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A KINETIC TEMPLATE EFFECT IN ARYLPHOSPHONIUM SALT FORMATION

by

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ABSTRACT

A Kinetic Template Effect in Arylphosphonium Salt Formation

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This thesis describes studies of a "kinetic template effect" which assists the formation of arylphosphonium salts from aryl halides and tertiary phosphines in the presence of a transition metal halide catalyst in refluxing ethanol. The "kinetic template effect" arises from the presence in the aryl halide of a limited range of ortho-substituents capable of intramolecular coordination with the metal at a critical stage of the reaction.

In Chapter One, the "kinetic template effect" is compared with the better known "thermodynamic template effect". Earlier work on related "kinetic template effects" in the formation of aryl-phosphorus bonds is reviewed. The evidence for the possible involvement of aryl-metal intermediates in such reactions is also discussed.

Chapter Two is concerned with the design and synthesis of potential template molecules. A model is proposed for the features necessary in the template substituent in terms of the nature and position of the donor atom or group essential for the replacement of the ortho-halogen under mild conditions.

Chapter Three describes a kinetic study of the nickel (II) catalysed reactions of ortho-haloaryl Schiff's base and ortho-haloarylazo-dyestuff templates with tertiary phosphines. A rate law is deduced which indicates a first order dependence in each reactant, i.e. rate α [template] [phosphine] [catalyst], an overall third order expression. Rate studies also indicate that the nature of the ortho-halogen is important, the order of replacement being I>Br>Cl. The effects of substituents remote from the ortho-haloaryl template are also considered. A mechanistic scheme consistent with the rate data is proposed.

The X-ray crystal structures of two arylphosphonium salts derived from template aryl halides are discussed in Chapter Four, providing unequivocal proof that the position of replacement of halogen in substrates bearing more than one replaceable halogen, in different positions, is ortho with respect to the template donor group.

C O N T E N T S

CHAPTER 3

A KINETIC STUDY OF THE NICKEL (II) ION-CATALYSED REACTIONS OF ORTHO-HALOARYL-SCHIFF'S BASE AND -AZO DYESTUFF TEMPLATES WITH TERTIARY PHOSPHINES

CHAPTER 4

CRYSTAL STRUCTURES OF TWO TETRAARYL-PHOSPHONIUM SALTS ISOLATED FROM TEMPLATE ASSISTED REACTIONS

ACKNOWLEDGEMENTS

COURSES AND CONFERENCES ATTENDED

PUBLISHED PAPERS

CHAPTER 1: INTRODUCTION

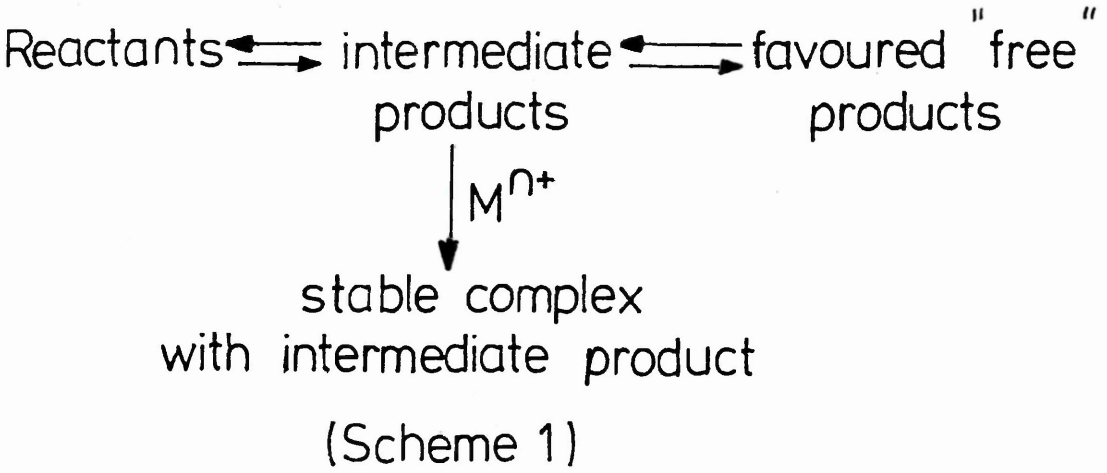
1.1 COORDINATION TEMPLATE EFFECTS

The reactions of coordinated ligands have been studied periodically since before the time of Werner.[1] However, only in the last 25 years has it been recognised that a metal ion should be able to exert a strong influence on the reactions of coordinated ligands, compared with those of the uncoordinated ligand, by causing changes in the ligand charge distribution. Having a metal present may lead to the enhancement of a particular reaction of the coordinated ligand or force a given reaction to occur by a different mechanism, or give a product not attainable without prior metal coordination. In addition, metal coordination may exert a "template effect", i.e. the coordination of ligands may place them in the correct geometry for their later union, thereby overcoming an unfavourable ΔS term for the reaction in the absence of the metal ion. Alternatively, metal coordination may stabilize a particular tautomer, which might not be stable or of little significance in the absence of the metal.

Two types of coordination template effect have been recognised. They are the "thermodynamic (or equilibrium) template effect" and the less common "kinetic template effect".

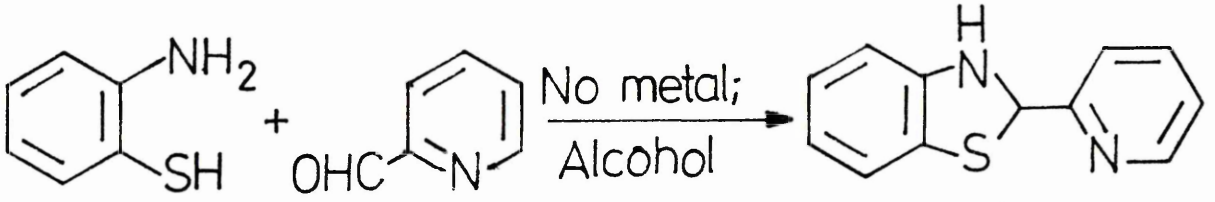
The "thermodynamic template effect" essentially involves the stabilization of an intermediate product in a thermodynamically directed process, i.e. it appears highly likely that these systems involve the sequestration

of the product of an equilibrium reaction, which would, in the absence of a metal ion, go on to the formation of a different final product[2] (Scheme 1).



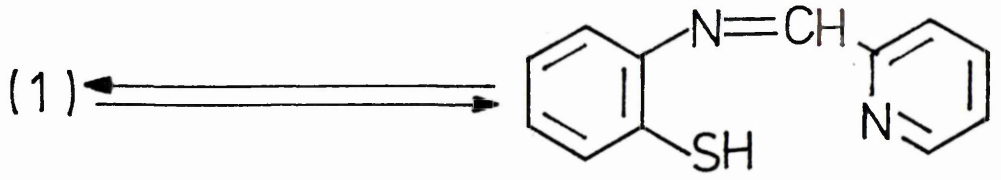
(Scheme 1)

Such is the case for 2-(2´-pyridyl)benzothiazoline (1) which is obtained by condensation of 2-aminobenzenethiol with pyridine-2-carboxaldehyde.[3-5]



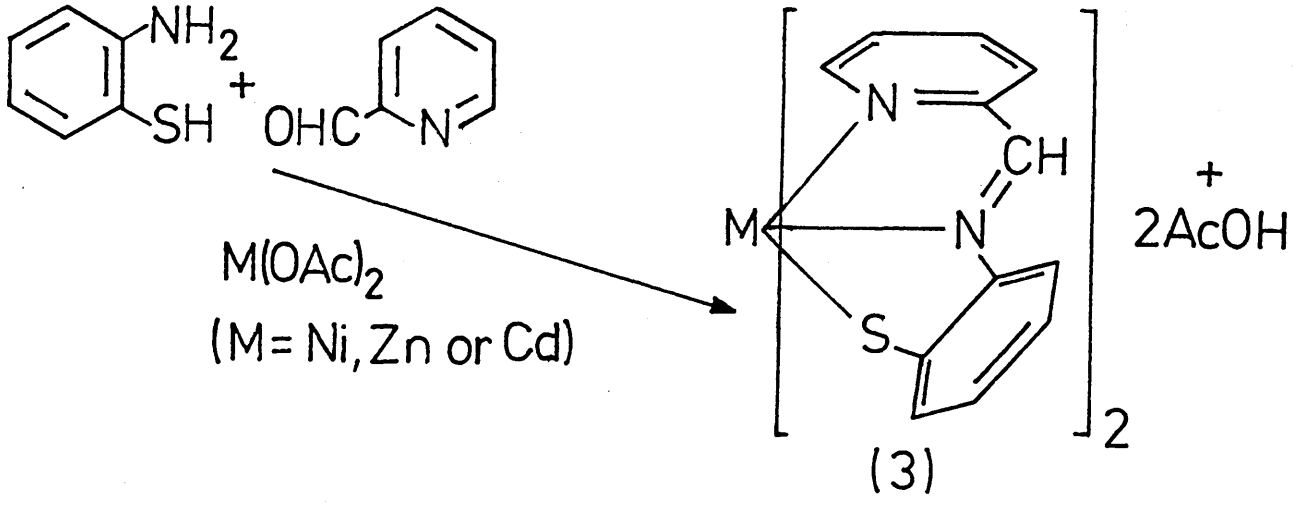
(1)
main product

The benzothiazoline (1) is in equilibrium with the tautomeric Schiff's base (2)



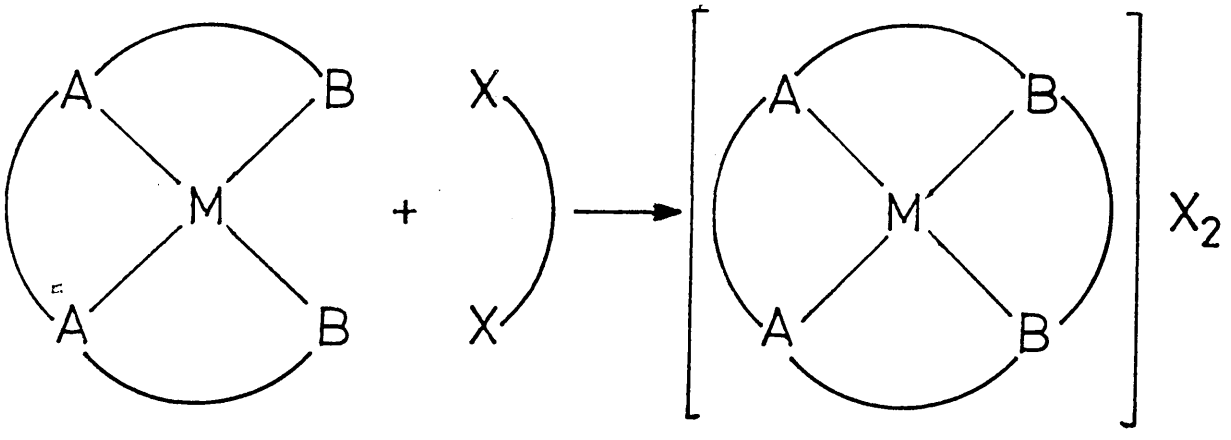
(2)

If the above reaction is carried out in the presence of a transition metal acetate, dark red Schiff's base complexes (3) of the Schiff's base tautomer (2) precipitate out.



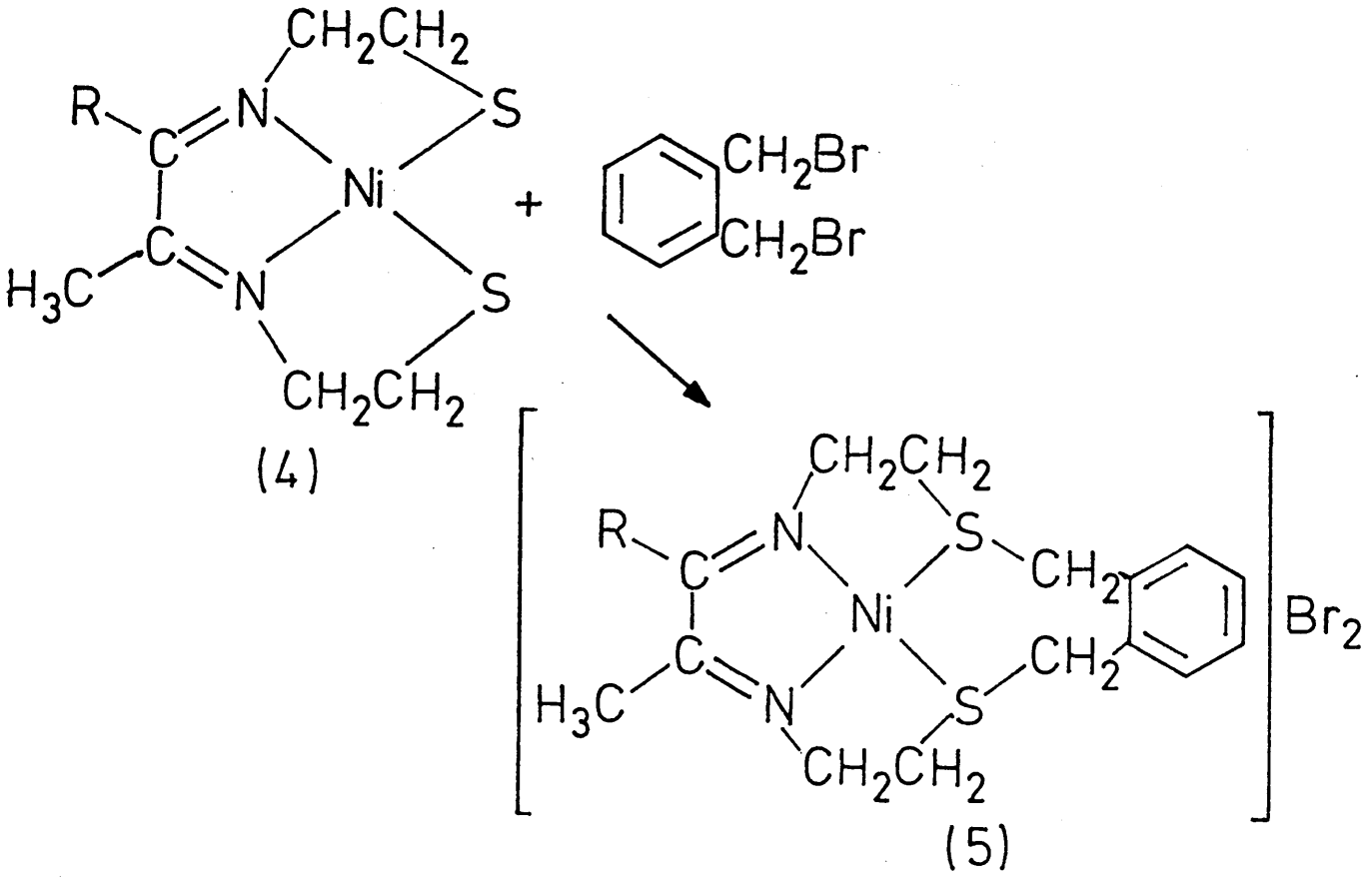
(3)

The "kinetic template effect" occurs when a metal ion holds groups within a substitution - inert complex in a proper array to facilitate a stereochemically selective multistep reaction, with the succession of reaction steps being determined by the metal ion.[6] (Scheme 2)



(Scheme 2)

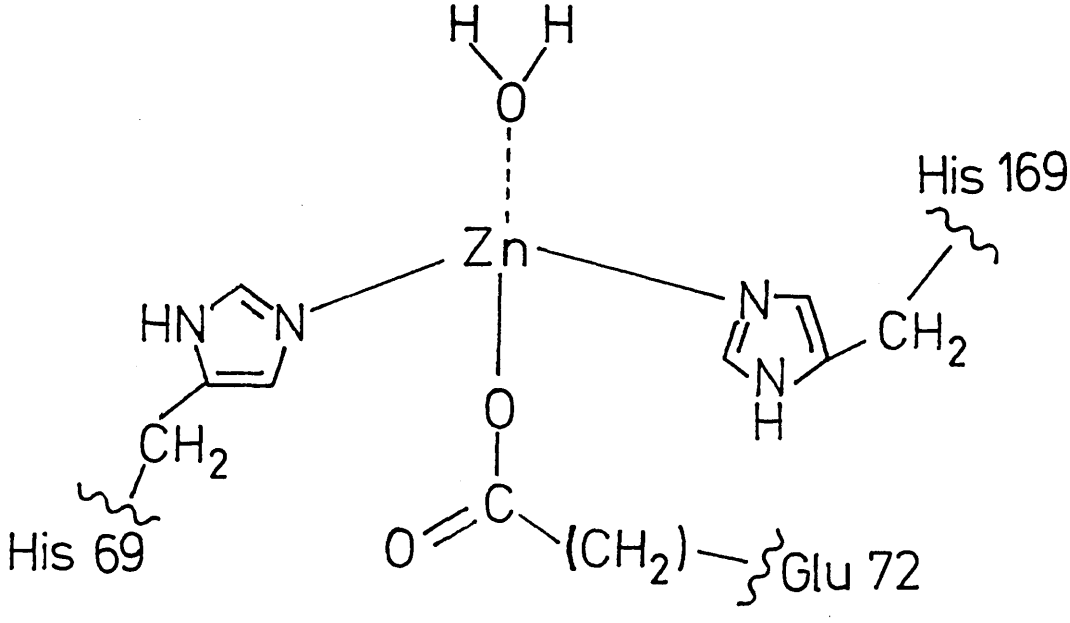
This effect is illustrated by the use of planar nickel (II) mercaptoethylimino complexes of type (4) where the terminal mercapto groups are held in cis-planar positions during the course of two step reactions with α,α′-dibromo-o-xylene to give the macrocycle (5)



(4) (5)

Examples of this type of "template effect" are extremely rare, except in the area of metalloenzyme chemistry. A specific example is provided by the group of enzymes known as Carboxypeptidases. These enzymes are zinc-containing globular proteins of RMM ∿ 35,000, which contain 1 mole of zinc per mole of enzyme. There are several forms of these enzymes which differ from each other in terms of the number of amino-acid residues in the chain (300-307). The enzyme carboxypeptidase A has received

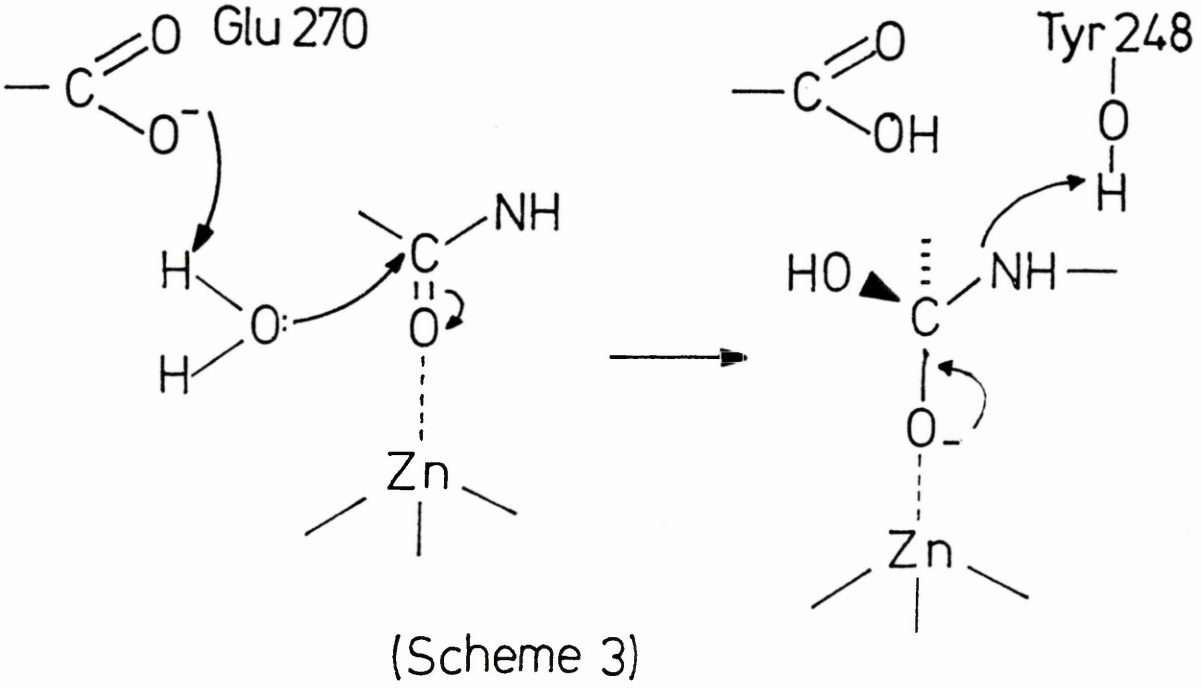
most study. Its activity is directed specifically to the hydrolytic cleavage of the C-terminal amino-acid residue of a peptide or protein. The enzyme is ellipsoidal in shape, containing a cleft in which resides the zinc and this, in fact, is the active site. X-ray studies show that the zinc (II) ion is involved in coordination to two histidine (His 69 and His 169), one glutamic acid (Glu 72) and one water molecule in a four-coordinate tetrahedral complex [7](6).



(6)

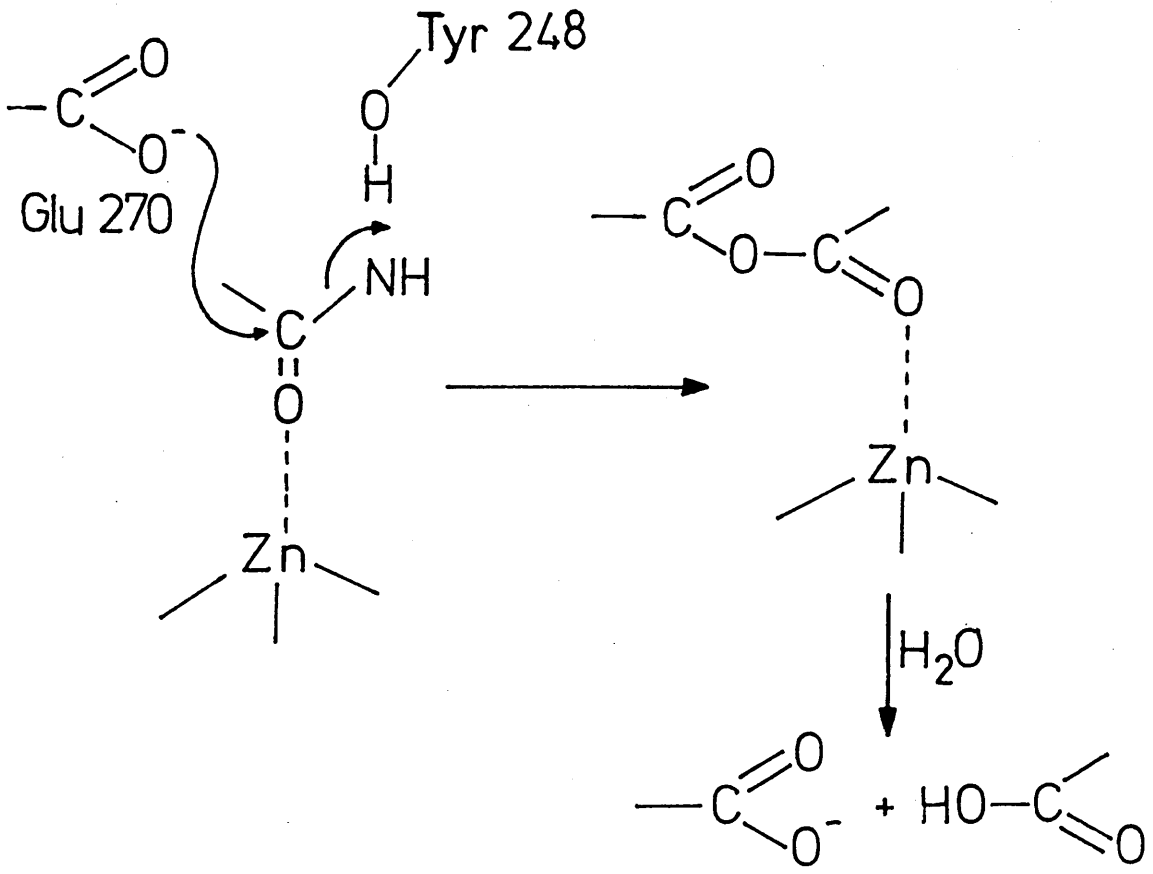
When the substrate enters the active site, the water molecule is displaced from the zinc, and the substrate is coordinated via an amide carbonyl group to the zinc ion. Some very subtle conformational changes occur in the active site involving glutamic acid (Glu 270) and tyrosine (Tyr 248), due to the "template effect" of the

zinc atom. The zinc ion enhances the polarization of the carbonyl group and makes the carbon atom more susceptible to nucleophilic attack by remaining water molecules activated by Glu-270. The resulting tetrahedral intermediate is protonated on nitrogen by Tyr-248 and can then decompose to amine and carboxylic acid. This is one view of the rather complex"zinc-carbonyl mechanism" [7] (Scheme 3).



(Scheme 3)

An alternative mechanism involves Glu-270 acting as a nucleophile rather than as a general base. In this instance a mixed acid anhydride intermediate is formed which is subsequently hydrolysed (Scheme 4)[7].



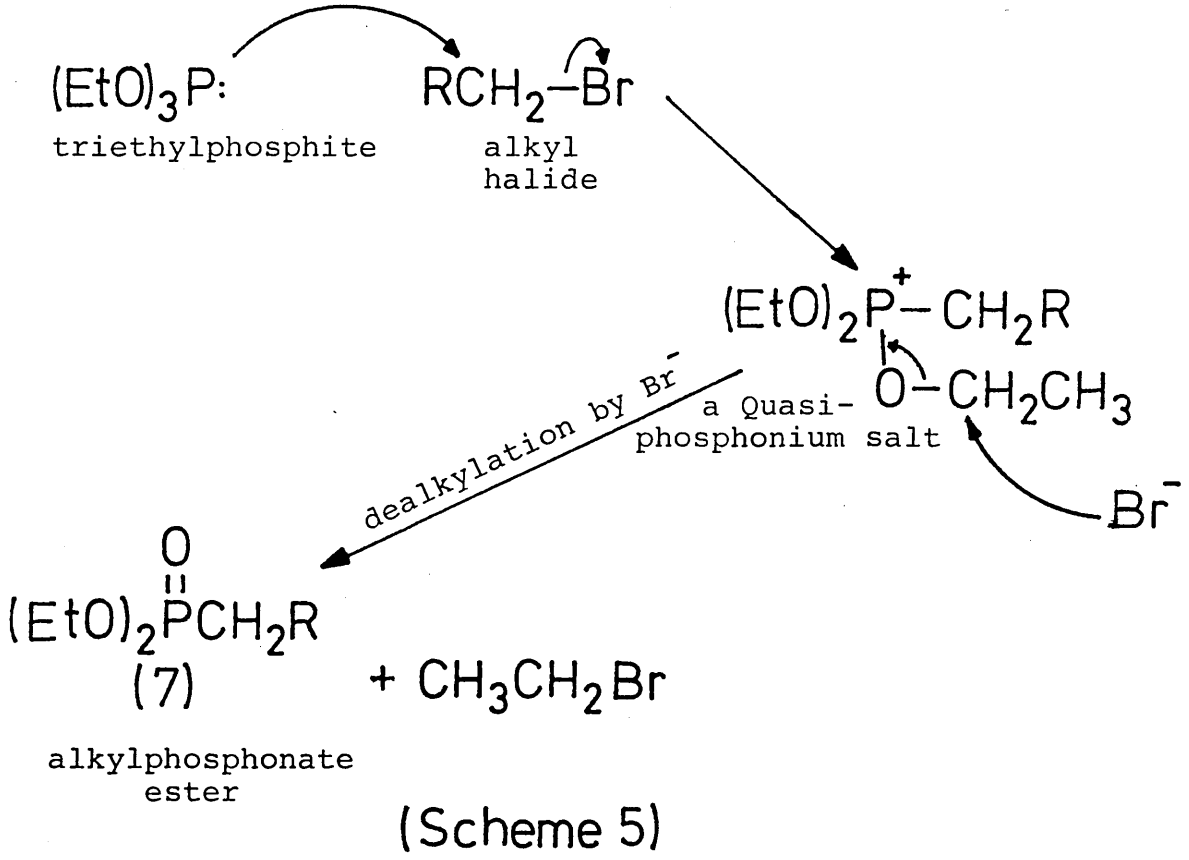
(Scheme 4)

1.2 METHODS OF FORMATION OF ARYL-PHOSPHORUS BONDS

The comparative ease with which alkyl halides undergo nucleophilic substitution with neutral tervalent phosphorus reagents facilitates the formation of alkyl-phosphorus bonds. Thus, e.g., the reactions of alkyl halides with tertiary phosphines readily yield alkyl-phosphonium salts[8], (eq(i)), and the related reactions of trialkylphosphites

$$R^1CH_2X + R^2_3P \longrightarrow R^1CH_2P^+R^2_3X^- \quad \text{.....(i)}$$

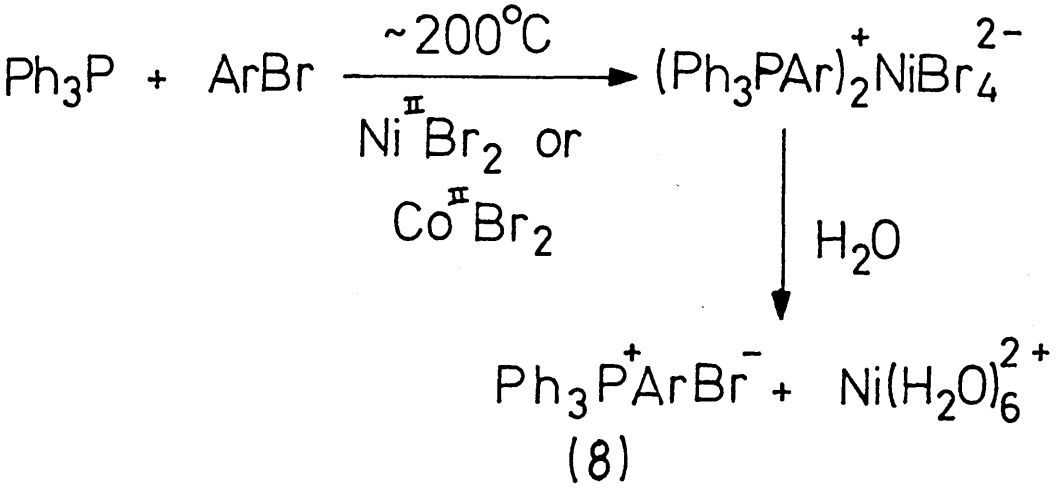
result in the formation of alkylphosphonate esters (7) (the Michaelis-Arbuzov reaction)[9-10] (Scheme 5).



(Scheme 5)

Attack by the nucleophilic phosphorus atom on an aryl halide would not normally be expected to lead to aryl-phosphorus bond formation, since unactivated aryl halides are unlikely to participate in S_N2 processes. Therefore a different strategy is required for the formation of aryl-phosphorus bonds from aryl halide substrates.

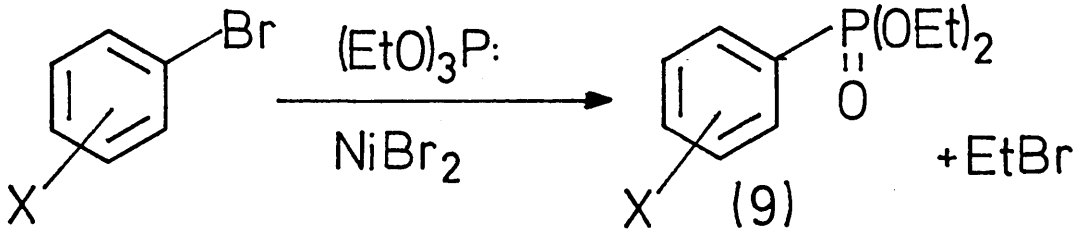
The formation of arylphosphonium salts (8) from the reactions of tertiary phosphines with simple aryl halides normally only proceeds at elevated temperatures (150-200°C) and in the presence of a transition metal salt, e.g., nickel (II) bromide or cobalt (II) bromide. This reaction is more commonly known as the Horner[11] reaction and usually proceeds in the absence of a solvent; however, these reactions have also been carried out in refluxing benzonitrile (b.p. 190°C).[12-14]



(8)

The formation of arylphosphonate esters (9) by the Tavs reaction is very similar to the Horner[11] reaction. The Tavs[15] reaction also uses a transition metal salt as

the catalyst but employs a phosphite rather than a tertiary phosphine in the production of the phosphonate ester (9).

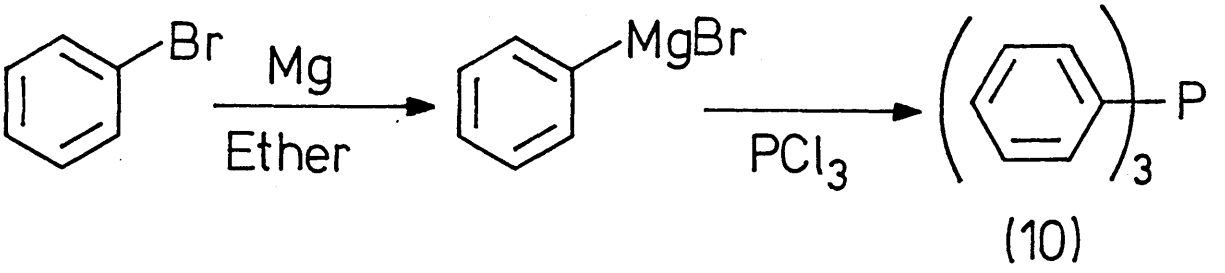


It is also known that a limited number of simple aryl-iodides and -bromides, on prolonged heating with trialkylphosphites at high temperatures, in the presence of copper bronze, undergo conversion to give moderate yields of dialkyl-arylphosphonates [16]. Reactions of these types are, however, limited in their application because of the sensitivity of substituents such as nitro, amino, hydroxy, etc., towards trialkylphosphites under these severe conditions.

Examples of "less-direct" methods leading to aryl-phosphorus bond formation involve the use of (a) Grignard reagents and (b) Phosphide anions.

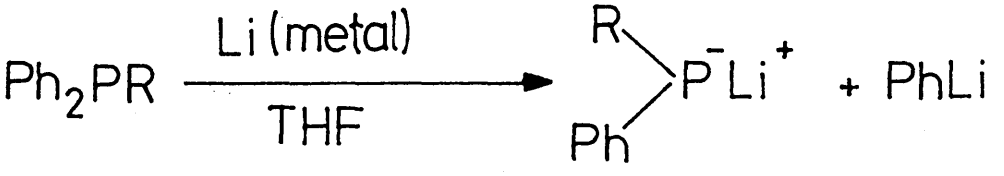
Tertiary phosphines, e.g., triphenylphosphine (10), are formed by the reaction of phosphorus trichloride with an excess of Grignard reagent [17] (phenylmagnesium bromide, derived from bromobenzene). This strategy relies on the attack of the carbanionic organometallic reagent at the electrophilic phosphorus atom. Excess Grignard reagent

is always employed so as to prevent the formation of the primary and secondary phosphines.

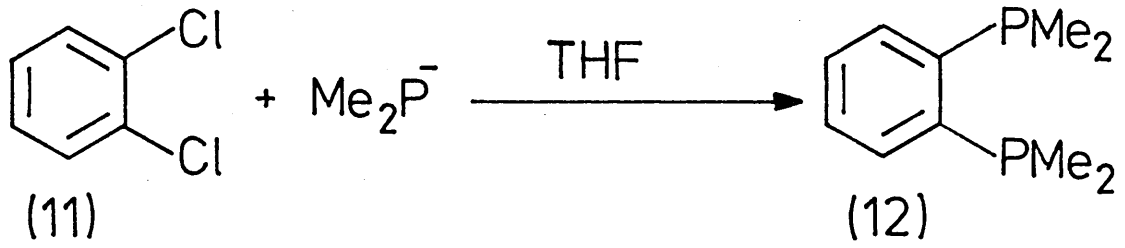


(10)

The other principal method of aryl-phosphorus bond coupling involves the use of phosphide anions (e.g. R_2P^- and RP^{2-}). These are very powerful nucleophilic species and are generated, for instance, by the addition of lithium metal to tertiary phosphines in a tetrahydrofuran (THF) solvent. The phenyllithium generated in this step can be removed by addition of tertiary-butyl chloride.

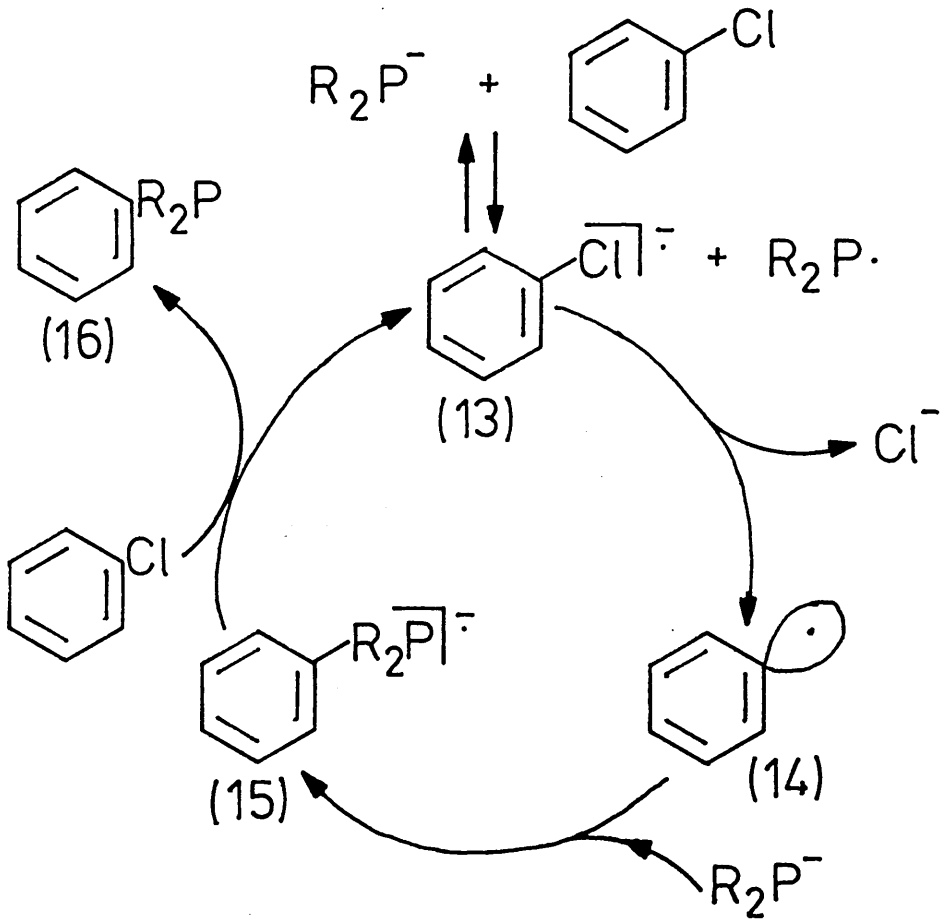


Phosphide anions in turn react with a wide range of alkyl halides, alkyl tosylates and <u>even</u> some aryl halides. An example of the latter involves the reaction of <u>o</u>-dichlorobenzene (11) with lithium dimethylphosphide [generated by the addition of dimethylphenylphosphine to a vigorously stirred suspension of lithium in THF] to produce the <u>o</u>-phenylenebis-(dimethylphosphine)[18] (12).



(11) (12)

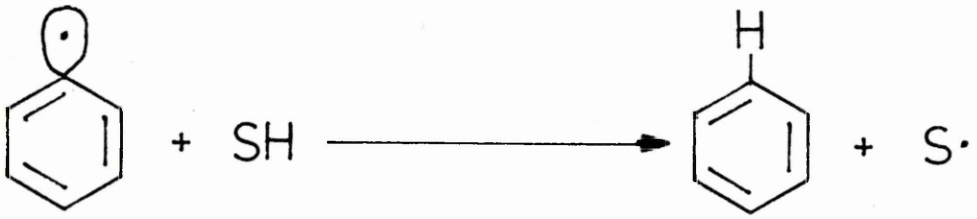
The mechanism of the formation of the o-phenylene diphosphine ligand (12) is unknown, but is almost certainly more complex than a straight-forward nucleophilic substitution process. It most probably involves the participation of radicals in an $S_{RN}1$ radical chain mechanism as summarised in Scheme 6 proposed by Kim and Burnett[19].



(Scheme 6)

An electron donor (e.g., a phosphide anion) is required to initiate the reaction to produce the radical anion (13). This, in turn, eliminates the halide ion to give the phenyl radical (14). Attack by another phosphide anion leads to the formation of a second radical anion (15), which then undergoes an exchange reaction yielding the product (16), plus the radical anion (13), thus completing the radical chain cycle.

The reaction can be terminated in a number of ways, examples of which are given below.

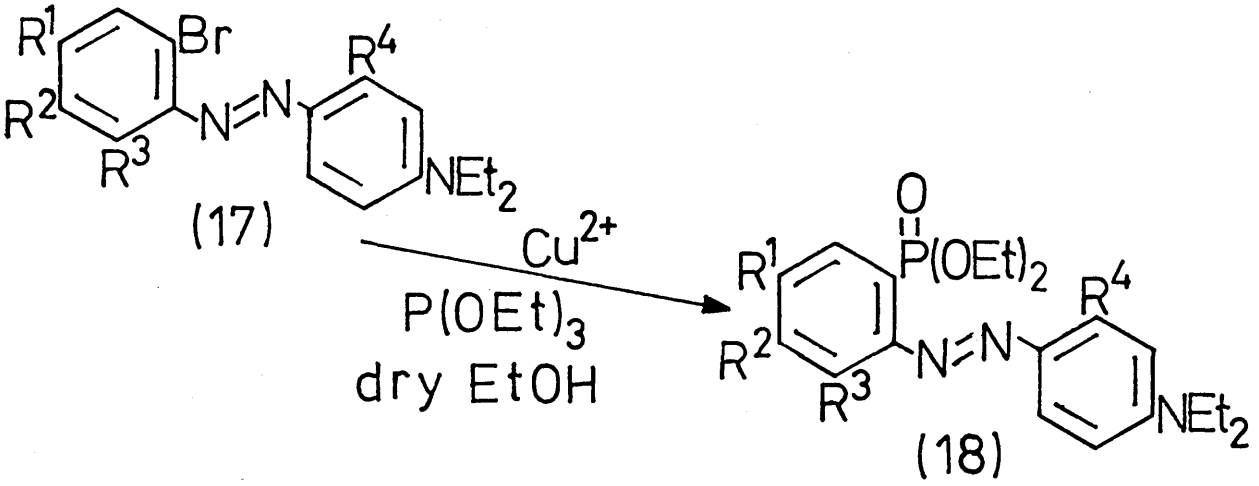


SH = Solvent

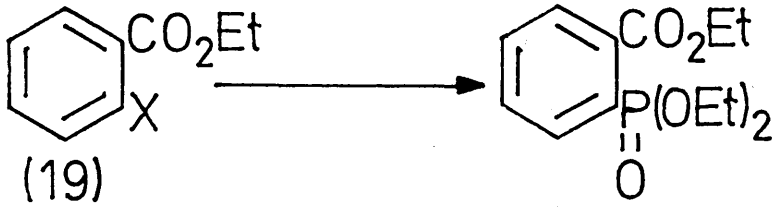
1.3 SURVEY OF THE LITERATURE RELATING TO THE KINETIC TEMPLATE EFFECT IN ORGANOPHOSPHORUS CHEMISTRY

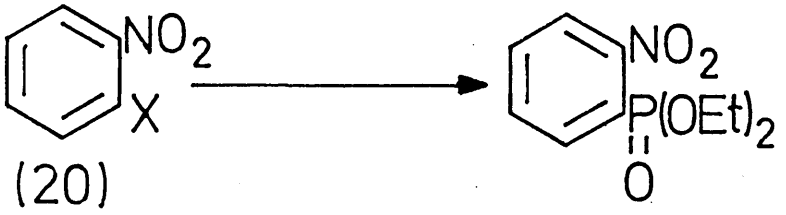
In 1979, Hall and Price [20], found that o-bromodiarylazo compounds (17;R^1=H,Me,NO_2 or Br,R^2 =H or NO_2,R^3 =H,Me,Et or NO_2,R^4 =H,NH_2 or NHCOMe) react with triethylphosphite in the presence of copper (II) acetate in boiling dry ethanol to give the corresponding o-diarylazo-phosphonate esters (18;R^1 =H,Me,NO_2 or Br,R^2 =H or NO_2,R^3 =H,Me,Et or NO_2 ,R^4= H,NH_2 or NHCOMe) in good yields.

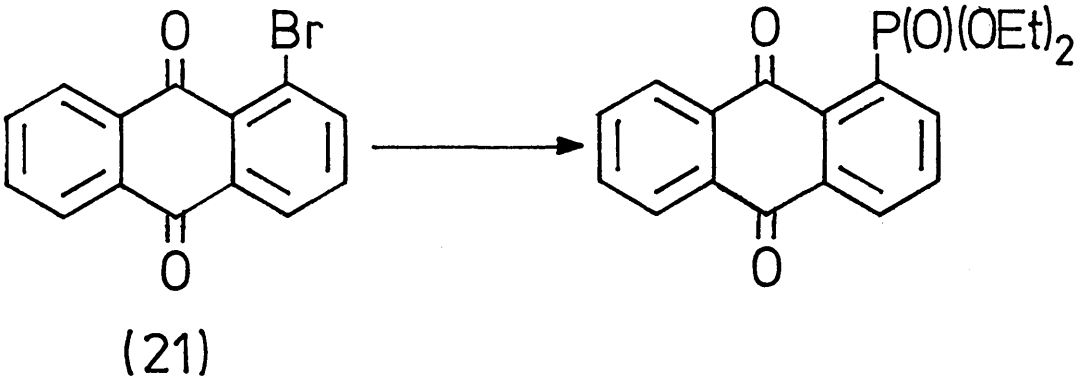
During initial studies, it was noted that in the reactions of the o-bromodiarylazo compounds (17) complete regiospecific replacement of the bromine atom ortho to the azo group occurs. A p-bromine substituent is unaffected. It was also found that the rate of the reaction is sensitive to steric effects of substituents in the phenyl ring carrying the bromine atoms (i.e. it was necessary that R^3 is any group other than hydrogen), but shows little response to their polar effects. In subsequent kinetic studies, it was observed that the presence of an additional acetylamino or amino group as substituent R^4 facilitates the reaction to a remarkable degree. The ease of halogen replacement follows the anticipated sequence [20], i.e. I > Br > Cl, with the iodo-compound reacting completely in 1 hour, the bromo- in 6 hours, and the chloro- in 24 hours. The fluoro- compound failed to undergo the reaction. The reactions do not proceed in the absence of copper (II) acetate.



The reaction has also been successfully applied to other aryl halides having ortho-donor substituents, e.g., the ethyl o-iodo- and o-bromo- benzoates (19; X=I or Br), o-iodo- and o-bromo-nitrobenzenes (20; X=I or Br) and 1-bromoanthraquinone (21), but fails with simple aryl halides.

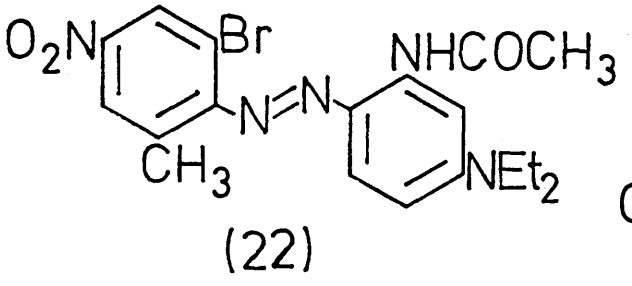






Conversion of aryl halide into phosphonate ester proceeds readily in other solvents such as dimethylsulphoxide, dimethylformamide and N-methyl-pyrrolidone, and more slowly in tetrahydrofuran and chloroform. Salts of other metals (e.g., iron, cobalt, nickel and zinc) fail to promote the reaction.

It was established that although such replacement reactions are facilitated by the presence of neighbouring donor atoms, they are in fact in competition with reductive dehalogenation and biaryl coupling reactions. Thus, for example, as well as isolating the phosphonate ester (23), Hall and Price also obtained the dehalogenated product (24) and the dimer (25) from the copper (II) acetate - promoted reaction of the azo dyestuff (22) with triethylphosphite.



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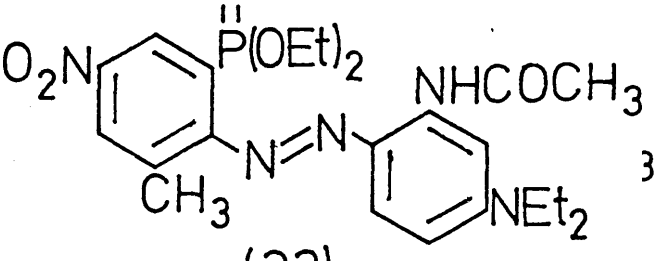

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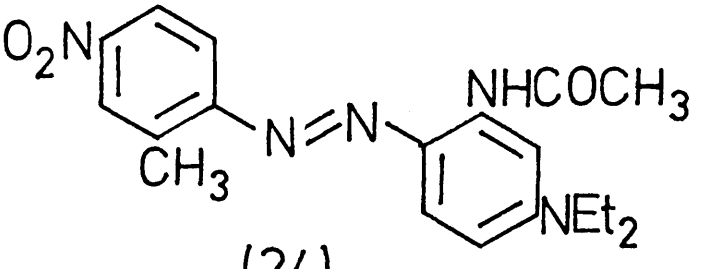

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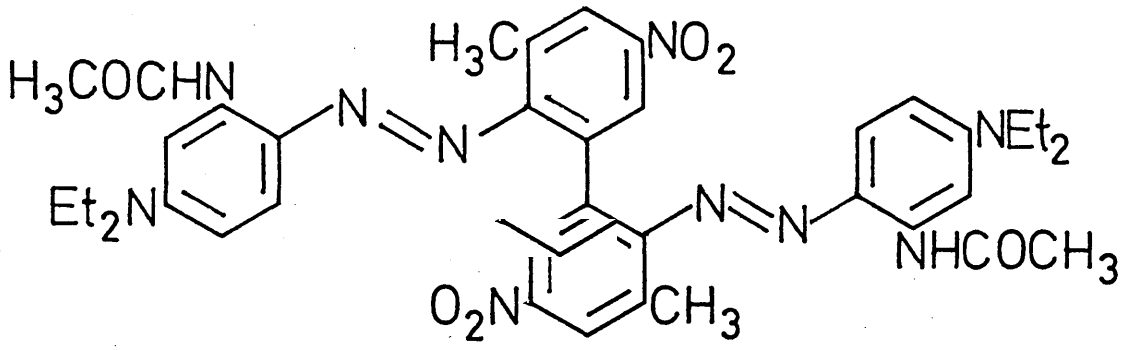


(25)

Factors influencing the outcome of the reaction are controlled by the choice of the catalyst and the solvent used.

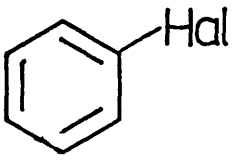
The function of the copper catalyst in promoting biaryl coupling, nucleophilic substitution, or reductive elimination of such aryl halides has been the subject of debate [21,22] for many years. Various mechanisms have been suggested [22-29] but none, however, satisfactorily account for all of the known facts.

In their study of the copper-promoted phosphonation reactions of azo dystuffs and related molecules, Hall and Price [20] classified aryl halides into three distinct groups:-

Type I,(26), in which the halogen does not occupy a potentially chelating position relative to any donor groups which may be present in the molecule.

Type II,(27), in which the halogen occupies a potentially chelating position relative to one donor group in the molecule.

Type III,(28), in which the halogen is so located relative to two donor groups in the molecule.



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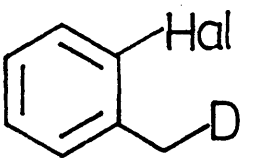

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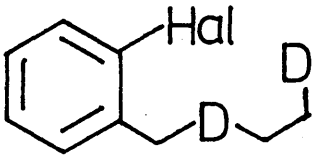
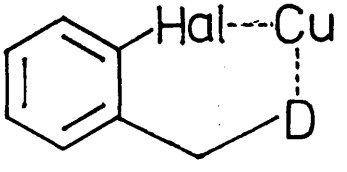


(28)

Furthermore, the results obtained by Hall and Price made it necessary to restrict the definitions of types II and III aryl halides to those in which the halogen atom is so located relative to a donor group in the molecule that, in principle, the possibility exists of its being involved in the formation of a six-membered chelate ring, involving the copper atom. These reactions therefore constitute an example of the involvement of a "kinetic template effect". However, to date, copper complexes based on types II and III halides ((29) and (30) respectively) have not been isolated as intermediates in reactions of this type.



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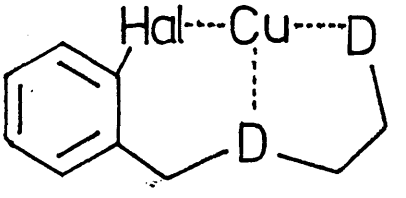
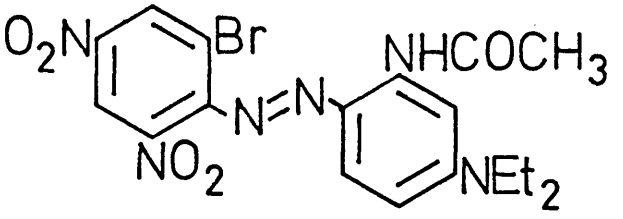


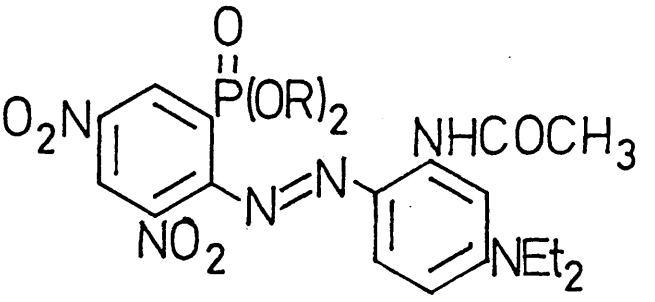
(30)

Hall and Price also discovered that the o-bromodiarylazo dyestuffs (31) undergo conversion to the corresponding dialkyl arylphosphonates (32; R=Me,Et,Pr^i,Pr^n,Bu,n-C_5H_{11}, n-C_7H_{15}) when treated with certain diesters of phosphorous

acid[30], in the presence of copper (I) iodide and sodium acetate in refluxing ethanol.

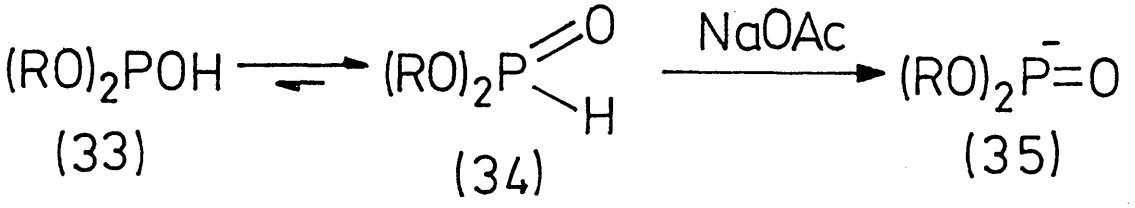


(31)



(32)

It is well known that dialkyl phosphites (33) exist mainly in the phosphoryl form (34) and are therefore unreactive in the Michaelis-Arbuzov reaction[9,10]. Addition of sodium acetate therefore generates the anions (35) <u>in situ</u> which readily combine with aryl halides in the presence of the copper (I) catalyst to give high yields of arylphosphonates (32).



(33) (34) (35)

Further investigations by Price et al[31] established that copper (II) alkanecarboxylates react with trialkyl phosphites in ethanol to form novel, pale blue-green complexes of type (36; R = Me or Et) from which derivatives containing bidentate ligands e.g., (37; R = Me or Et; bipy ≡ 2,2´-bipyridyl) could also be prepared[32].

$$\left[Cu_3(O_2CMe)_5\{P(OR)_3\}_2 \right] \text{——— (36)}$$

$$\left[Cu(O_2CMe)\{P(OR)_3\}(bipy) \right] \text{——— (37)}$$

Derivatives of type (38) were obtained by treating (36; R=Et) with a unidentate ligand such as pyridine.

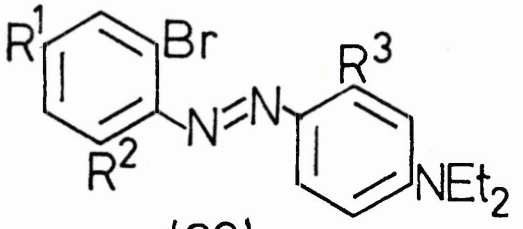
$$\left[Cu(O_2CMe)\{P(OEt)_3\}_2 \right]$$

(38)

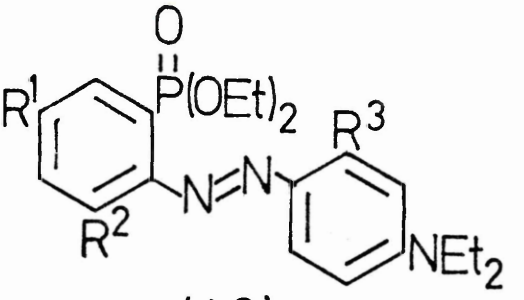
These workers also noted the distinction between aryl halides of types II and III in the rates of their reactions with the complex (36; R=Et). The type III system was found to undergo the reaction ca one hundred times faster than the type II system, thus suggesting that the presence of two donor atoms in systems of type III provides more favourable circumstances for coordination than the single donor atom present in the type II substrates.

Price demonstrated that each of these complexes is able to effect the phosphonation of certain aryl halides at room temperature in solution, in the absence of any added phosphite. A kinetic and mechanistic study was subsequently undertaken of the reactions of the above

complex (36; R=Et) and a series of azo dyestuffs of type (39;R^1= Br or NO_2; R^2= Me, H or NO_2; R^3= NHCOMe, H or Me)



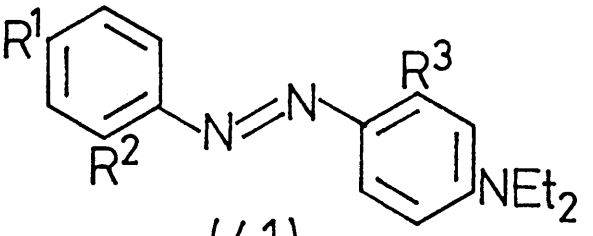
(39)



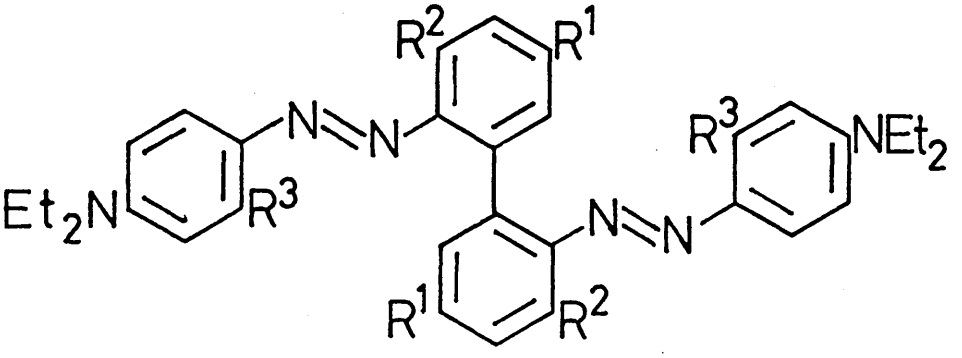
(40)

Kinetic data for the phosphonation of the azo dyestuffs (39; R^1= NO_2; R^2 = NO_2; R^3 = NHCOMe) using the complex (36; R=Et) to give the phosphonate (40; R^1 = NO_2; R^2 = NO_2; R^3 = NHCOMe) were obtained by hplc analysis. The phosphonation reaction was found to be an equal concentration second order process. As well as providing a means of detection of the phosphonate ester (40), the hplc method simultaneously showed that the yields of the reductive substitution product (41; R^1 = NO_2; R^2 = NO_2; R^3 = NHCOMe) and the dimer (42; R^1 = NO_2; R^2 = NO_2; R^3 = NHCOMe) decreased at the same time as both the temperature of the reaction and the rate of phosphonation increased. This suggested that compounds (41) and (42) are kinetically favoured products and that the phosphonate ester (40) is thermodynamically favoured. It also indicated that the three products had possibly originated from a common intermediate.

The addition of a radical scavenger, 1,1´-diphenyl-2-picrylhydrazyl (dpph), resulted in the complete suppression of the formation of the biaryl coupling product (42) and

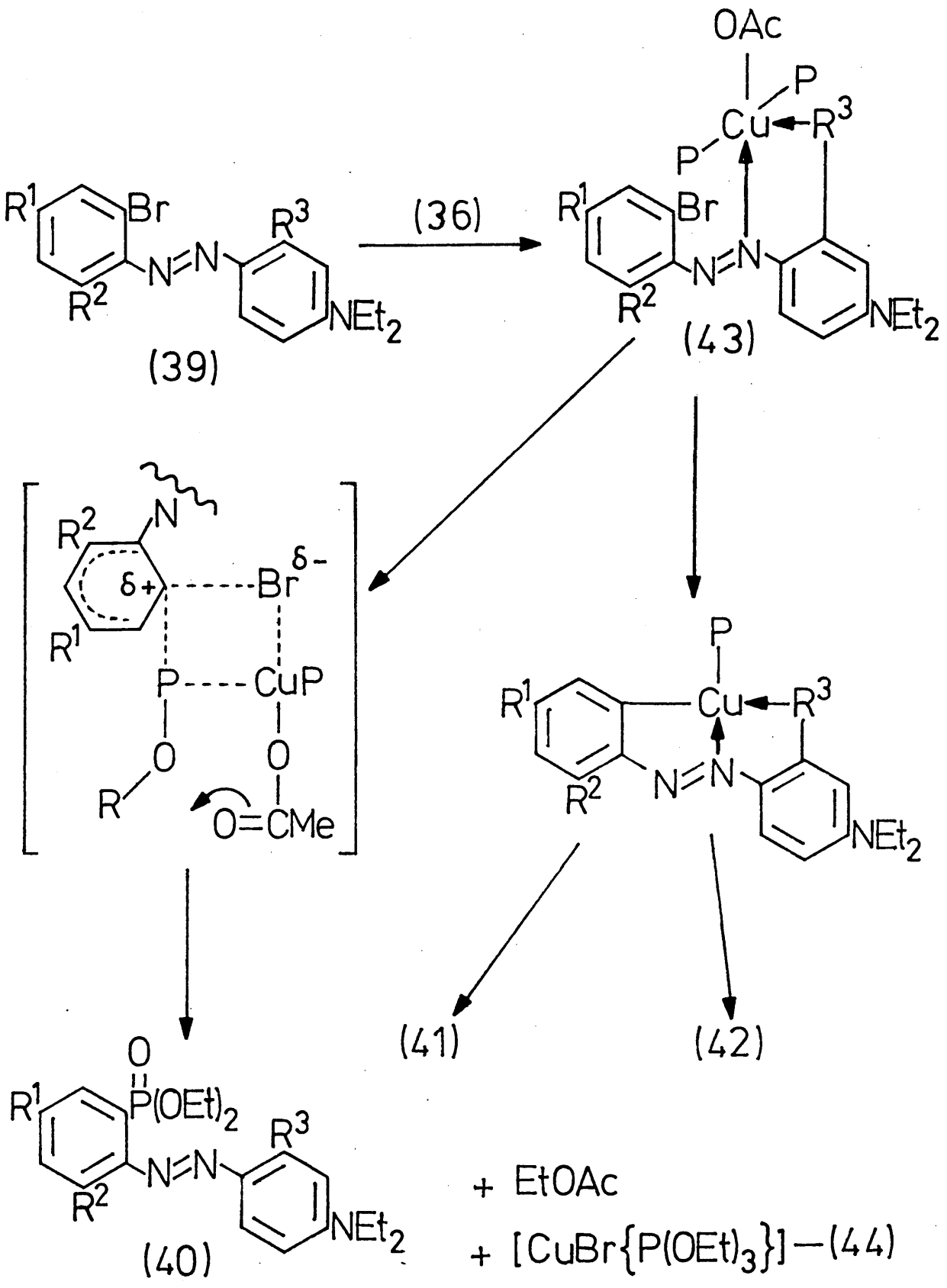


(41)



(42)

also strongly inhibited the formation of the reductive substitution product (41). Further support for the intervention of radicals was obtained when the above reaction was performed in the absence of light, and similar observations were made. The role of the solvent in the phosphonation reaction was also significant. When carried out in tetrahydrofuran (THF) at room temperature, phosphonation was no longer a simple second order reaction, and the formation of the phosphonates occurred more slowly in THF than in ethanol. The reaction in THF was accompanied by a significant increase in the yields of biaryl coupling and reductive substitution products, suggesting that solvent cage effects are important in such radical type reactions.

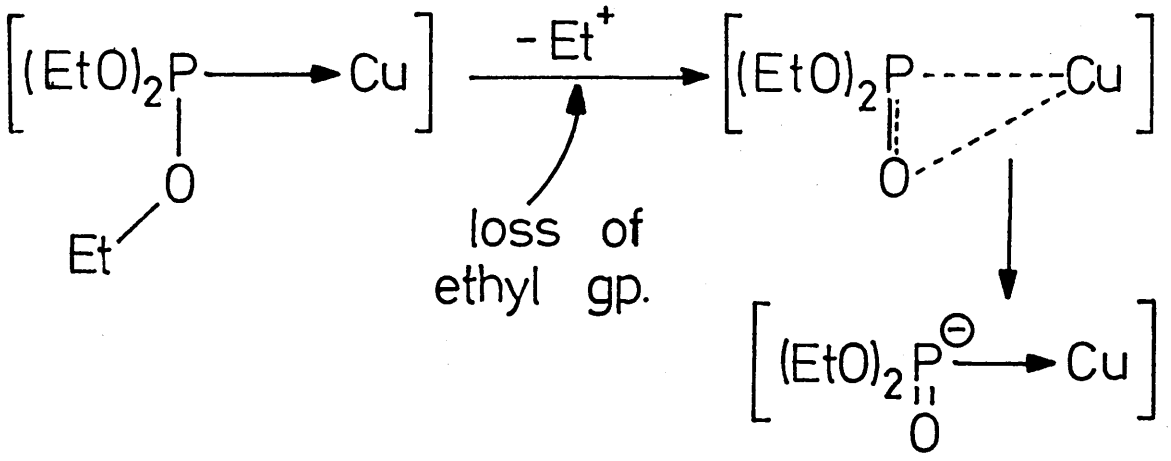

OAc
P
Cu
R3
P
R1
Br
N=N
R2
NEt2
(36)
(39)
(43)
δ+
δ-
Br
P
CuP
O
O
R
O=CMe
(41)
(42)
O
P(OEt)2
(40)
+ EtOAc
+ [CuBr{P(OEt)3}]—(44)

(Scheme 7)

At this stage of the research, Price et al [32] attempted to rationalise the observations they had made, and proposed a mechanistic scheme which would account for the appearance of each of the products (40), (41) and (42), based on the idea that they must originate from a common intermediate (43), (Scheme 7).

Since the stoichiometric phosphonation reactions were carried out in the absence of any free (or added) phosphite ligand, it was evident that phosphonation must occur within the coordination sphere of the metal atom. The products of the reaction between the aryl halide (39) and the complex (36; R=Et) included $[CuBr\{P(OEt)_3\}]$ (44) and ethyl acetate, in addition to (40), (41) and (42). This suggested that the common precursor (43) (which was not isolated) contained both copper and the aryl halide, as shown in Scheme 7. The fact that the ethyl group was displaced from the triethyl phosphite and isolated as ethyl acetate, and that the bromine lost from (39) was isolated in the copper complex (44) was said to be consistent with a concerted nucleophilic attack on the coordinated phosphite, which is thereby transformed into the phosphonate (40). Such a conversion is probably accompanied by a coordination isomerisation as shown in Scheme 8.

This subsequent re-arrangement would generate a negative charge at the phosphorus atom, which would attack the carbocationic centre in the carbon-halogen bond of the aryl halide (39).



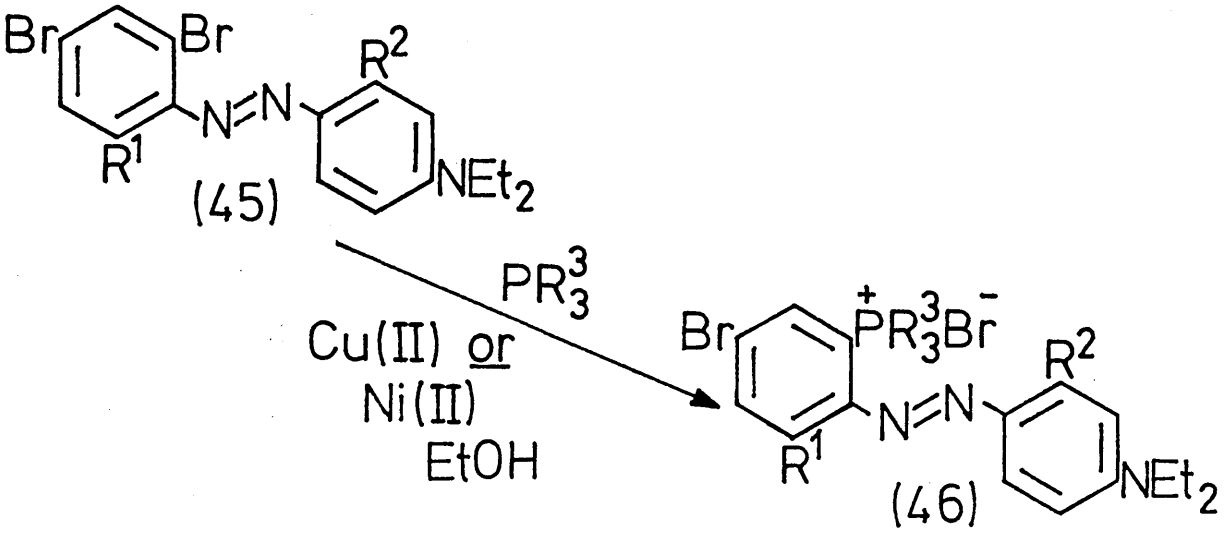
(Scheme 8)

A recent review of the nucleophilic aromatic substitution reactions of aryl halides in the presence of copper complexes has been published[33]. Marked activation of the halogen atom induced by the presence of a potential donor group in the ortho position is a common occurrence and substitution of the halogen in o-halodiarylazo compounds has been achieved under mild conditions with a variety of other nucleophiles, e.g., -OR (R=H)[34], (R=alkyl or aryl)[35]; -NHR (R=H or aryl)[35], (R=alkyl)[35,36]; -CN[37]; $-SO_2R$[35,38] and $-NO_2$[39].

Following the work of Price et al, Allen et al decided to investigate the reactions of a related series of dye stuffs with a range of tertiary phosphines in the presence of metal ions, with the goal of preparing novel diarylazo-phosphonium salts, of possible application as cationic dyes.

Allen et al [40,41] have shown that when the o-bromo-diarylazo compounds (45; R^1 = H or Me; R^2 = H or NHCOMe) are heated under reflux in ethanol with a range of tertiary

phosphines in the presence of a catalytic amount of either copper (II) acetate or nickel (II) bromide, the related diarylazophosphonium salts (46; R^1 = H or Me; R^2 = H or NHCOMe; R^3 = Bu, Ph, 2-thienyl, 2-furyl) are formed in good yields.

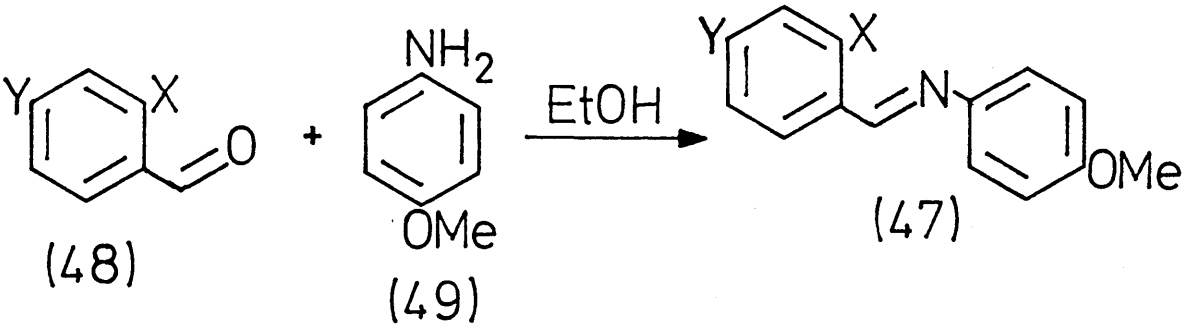


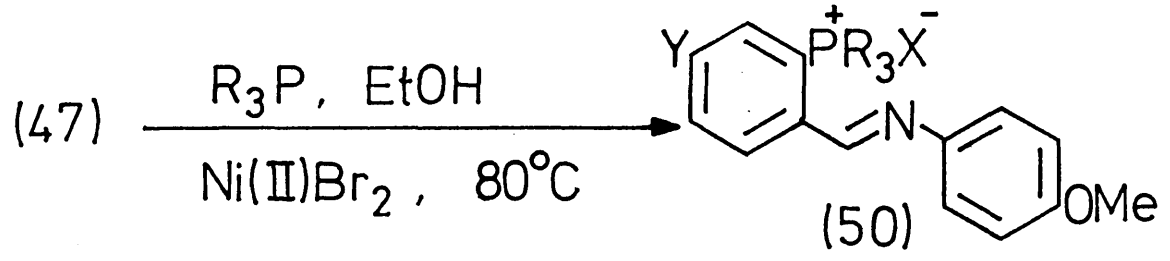
There are similarities with Price's discoveries in that these reactions proceed under similarly mild conditions with the complete regiospecific replacement of the halogen ortho to the azo group. The para-halogen is unaffected. In the absence of the metal catalyst, the replacement reaction does not occur. Allen et al have suggested [40,41] that these reactions (and the related phosphonation reactions) involve the operation of a "kinetic template effect", in which metal ion promoted replacement of the halogen ortho to the azo group is assisted by coordination of the metal to an azo nitrogen group.

In order to explore the scope of the operation of such "kinetic template effects" in promoting the formation of aryl-phosphorus bonds, studies of the reactivity towards

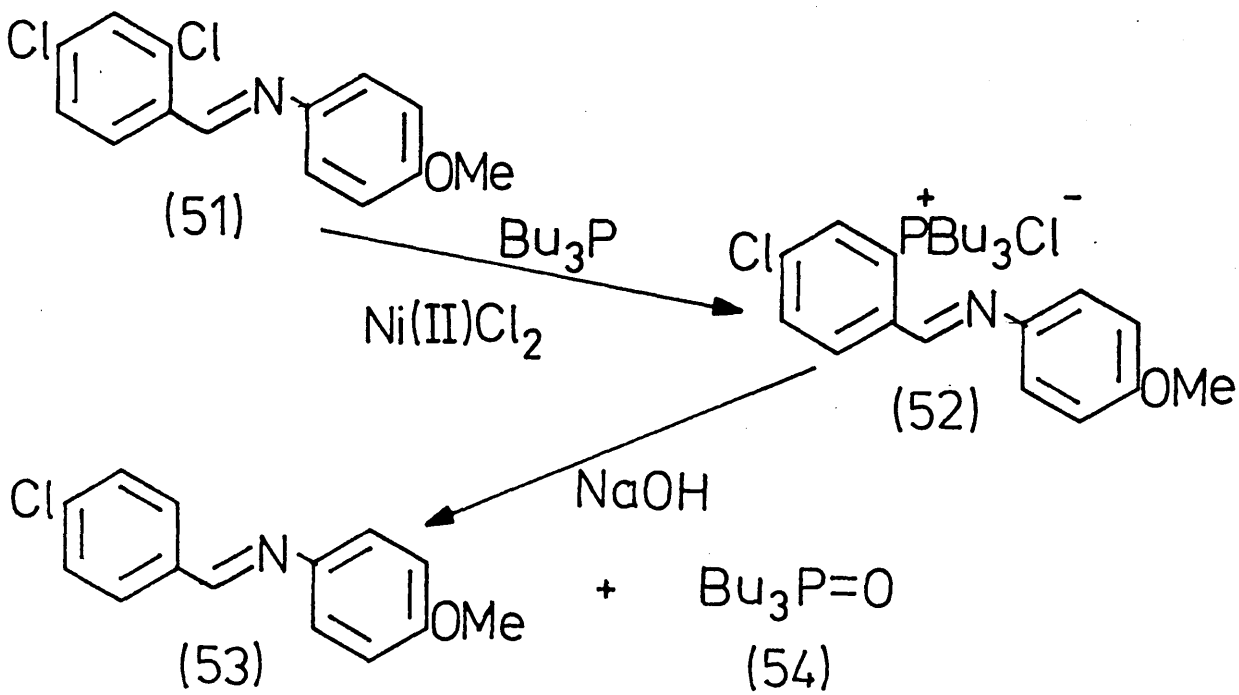
tertiary phosphines of a wider range of aryl halides bearing donor substituents in the ortho position have been carried out. These aryl halides also have the potential to co-ordinate to a metal ion catalyst and thereby perhaps promote facile replacement of the halogen under mild conditions.

Studies [40,41] have been undertaken of the related reactions of a series of Schiff's bases of type (47; X=Cl, Br or I; Y=H or Cl) derived from the reactions of halogeno-benzaldehydes (48; X=Cl, Br or I; X=H or Cl) with para-anisidine (49). On treatment with triphenylphosphine or tributylphosphine in refluxing ethanol in the presence of a catalytic amount of nickel (II) bromide, the salts (50; R=Bu or Ph; X=Cl, Br or I; Y=H or Cl) are formed over several hours.

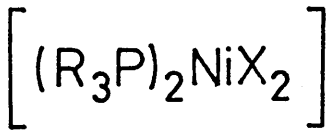




Preliminary comparative rate studies using a conductiometric technique indicated that the ease of replacement of the ortho halogen is I > Br > Cl which compares well with Price's results [20]. The related o-fluoro-compounds do not undergo this reaction. The isomeric p-halocompounds (47; X=H; Y=Cl, Br or I) also do not react under these conditions. The dichloro Schiff's base (51) undergoes a regiospecific replacement of the ortho chlorine atom to give the salt (52). Unambiguous proof that the o-chlorine atom was replaced was provided by alkaline hydrolysis of the tributylphosphonium salt (52), which proceeds with cleavage from phosphorus of the group most stable as a carbanion [42,43] to give the para-chloro Schiff's base (53), together with tributylphosphine oxide (54). The above reactions of the Schiff's bases also proceed in acetonitrile and in methanol, but at a slower rate than in ethanol, and also to some extent in tetrahydrofuran and chloroform.

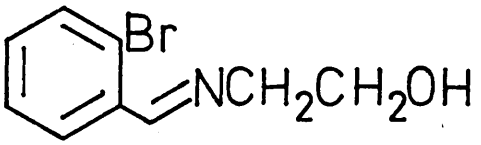


The reactions of equimolar amounts of preformed bis(phosphine)nickel (II) halide complexes (55; R = Bu or Ph; X = Cl, Br or I) with the o-halogeno Schiff's bases lead to a much faster rate of formation of the phosphonium salts. Apart from nickel (II), no other metal has been found which significantly catalyses the reaction.

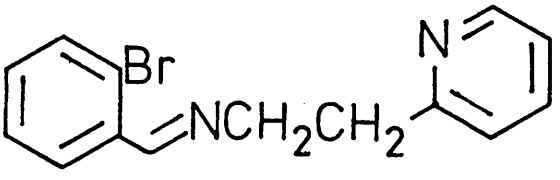


(55)

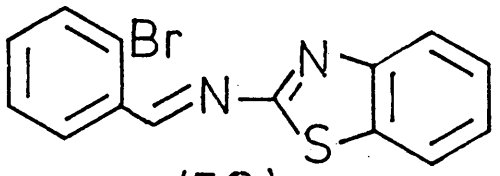
Introduction of a second donor site (c.f. R^3 in the azo compound (39) into the imino moiety of the Schiff's bases is found to inhibit the reaction. Thus the Schiff's bases (56-59) fail to undergo the substitution reaction on heating with triphenylphosphine in ethanol containing a catalytic amount of nickel (II) bromide or in the presence of an equimolar amount of a preformed bis(phosphine)nickel (II) halide complex (55). Such results suggest that when the Schiff's base bears a second donor group which is capable of co-ordinating with the metal ion, especially when the formation of a chelate complex is possible, then the metal ion is diverted from its catalytic role. This scenario therefore differs from that of the dyestuff phosphonation reaction.[20]



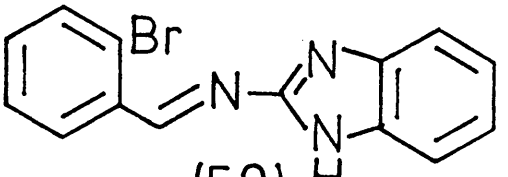
(56)



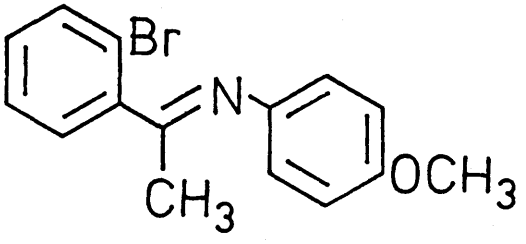
(57)



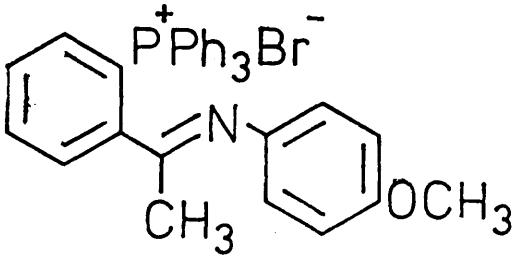
(58)



(59)

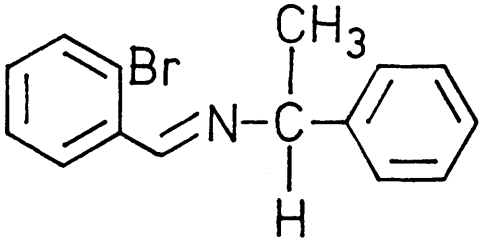


(60)

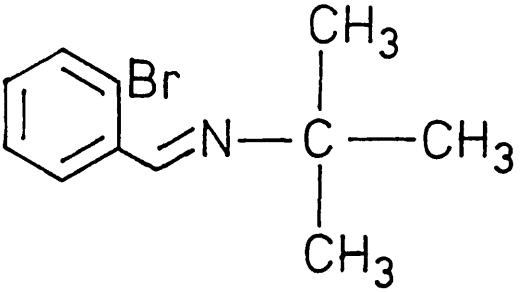


(61)

The Schiff's base (60) derived from the reaction of o-bromoacetophenone with p-anisidine, also undergoes the replacement reaction to give the salt (61), the presence of the methyl group on the azomethine carbon causing no steric effect. However, increased steric crowding at the azomethine nitrogen is found to inhibit the reaction; thus, e.g., (62 and 63) fail to undergo the substitution reaction.

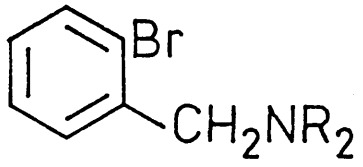


(62)

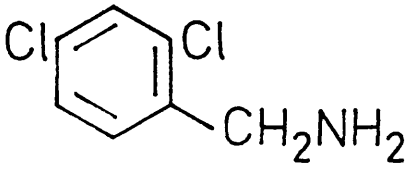


(63)

The very critical nature of the donor atom and its position with respect to the ortho halogen for the promotion of a template-assisted reaction is illustrated by studies of the reactivity of a number of related systems[44]. It has been established that o-halogeno-benzylamines of types (64; R = H or Me) and (65), whilst having a nitrogen atom in the same relative position as in the reactive Schiff's bases, also fail to undergo conversion to the related phosphonium salts.

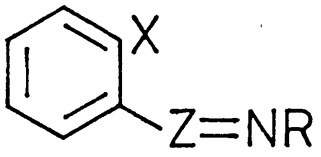


(64)



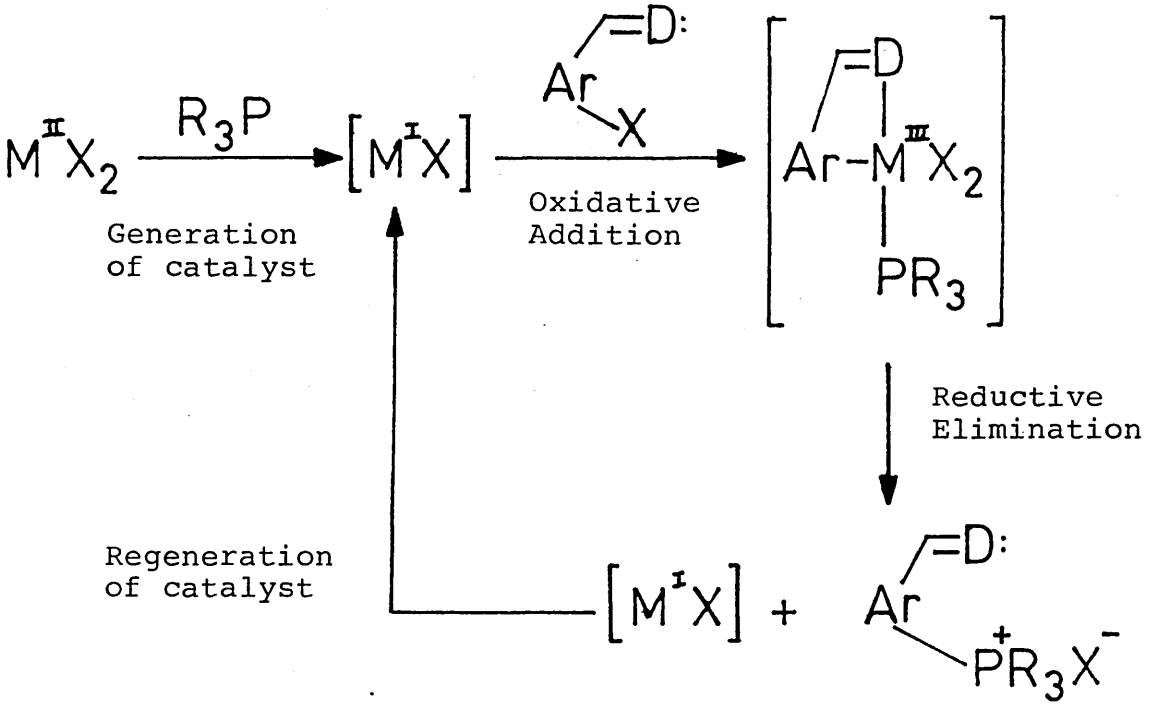
(65)

Thus it would appear that such metal-ion promoted substitution reactions require a very specific template of type (66; Z = CH or N; X = Cl, Br or I; R = non-sterically crowded alkyl or aryl group) in which the nitrogen is sp^2-hybridised.



(66)

Unlike Price's earlier classification of a type II aryl halide (27), it would appear that the donor atom must possess some form of Π-acceptor character. It is of interest to note that the reactions of the diarylazo template systems (39)[20] appear to be much less sensitive to the presence of additional donor centres (e.g. R^3 = NHCOMe) than those of the Schiff's bases, and also that the reactions of the former are catalysed by both copper (II) acetate and nickel (II) bromide, whereas nickel (II) is required specifically for the reactions of the Schiff's bases. Clearly some very subtle co-ordination chemistry is involved in these reactions. It has been suggested that it is highly probable that electron transfer processes[45] are also involved, in which the metal ion is initially reduced to a lower oxidation state, e.g. Ni^1 (the active catalytic species) which then undergoes a co-ordination template assisted oxidative insertion into the carbon-halogen bond to form an aryl-nickel (III) intermediate, followed by formation of a phosphorus-carbon bond in a reductive elimination step, giving the phosphonium salt with regeneration of the nickel (I) catalyst as shown in Scheme 9.

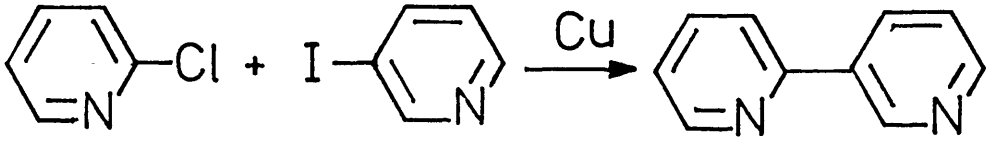

M^II X2
R3P
[M^I X]
Generation of catalyst
Ar
X
=D:
Oxidative Addition
Ar-M^III X2
PR3
Reductive Elimination
Regeneration of catalyst
[M^I X] +
Ar
=D:
P^+R3 X^-

(Scheme 9)

1.4 THE POSSIBLE INVOLVEMENT OF ARYL-METAL INTERMEDIATES IN THE METAL-CATALYSED FORMATION OF ARYL-PHOSPHORUS BONDS

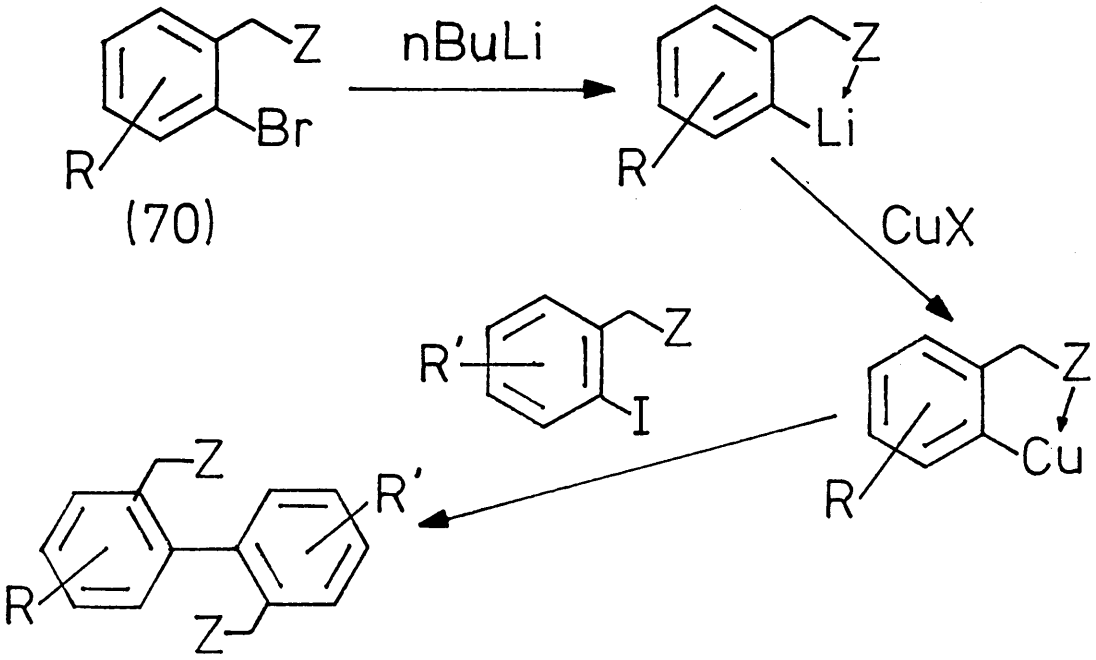
The mechanisms suggested in section 1.3 for the template -assisted formation of arylphosphonium salts involve the formation of aryl-copper and aryl-nickel derivatives. In view of this, a survey of some other reactions which are also thought to involve such species is considered relevant.

The observations by Ullmann that copper and its compounds can both promote nucleophilic substitution of aryl halides[46] and assist coupling of aryl halides to form biaryls[47] have been developed so that these are now important and widely used procedures in organic chemistry.[48] Indeed, one major advantage of the Ullmann reaction in modern organic chemistry is that unsymmetrically substituted arenes may be coupled easily. It is now common practice to react an activated aryl halide with another which is relatively inert. Thus, for example, the slow addition of 2-chloropyridine (67) to a suspension of copper powder in N,N-dimethylformamide containing 3-iodopyridine (68) affords 2,3′-bipyridyl (69) in moderate yield.[49]



(67) (68) (69)

In yet another variant, Zeigler et al[50] have developed a technique which achieves a low temperature and consistently productive coupling reaction between unsymmetrical aryl halides. Here, a copper (I) aryl species (70; Z=NR_2 or SR) stabilized intramolecularly by a heteroatom, is generated from one aryl halide and then reacts with another aryl halide bearing an ortho substituent which may also function as a ligand. The strategy is summarized in Scheme 10.

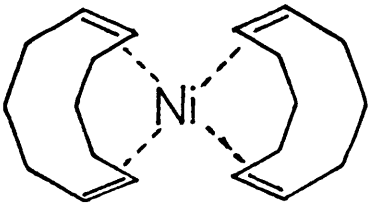


(Scheme 10)

This concept of intramolecularly ligand-stabilized aryl-transition metal complexes[51,52] has been exploited previously, but only to couple symmetrically - substituted aryl halides.

Classical Ullmann reaction procedures are still commonplace in the literature of organic chemistry, but for some symmetrical biaryl syntheses, the use of zerovalent nickel

reagents appears to be more productive. Semmelhack's[53] original discovery utilizes isolable bis(1,5-cyclooctadiene) nickel (0),(71), or tetrakis(triphenylphosphine)nickel (0), (72) as catalysts - both of which are air sensitive and difficult to prepare.



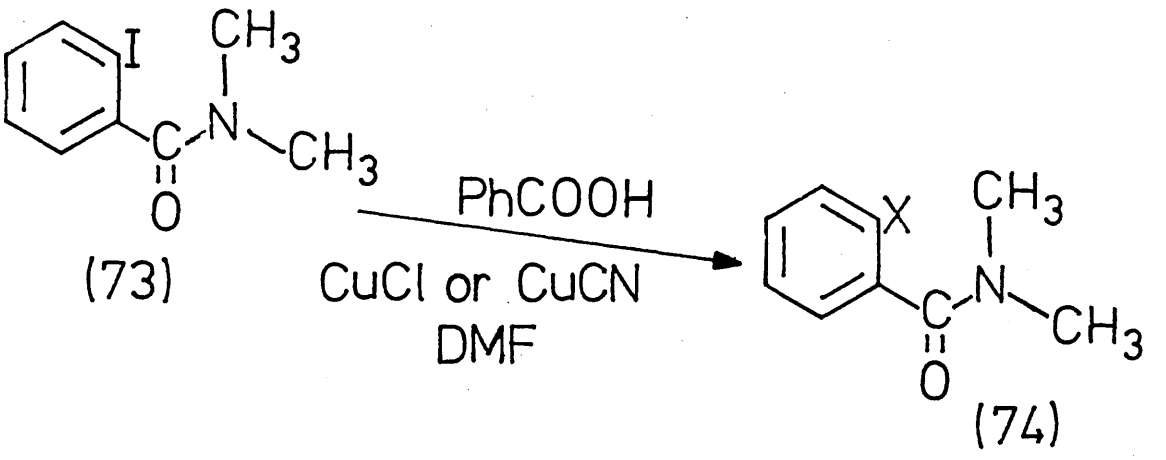
(71)

$[(Ph_3P)_4Ni]$

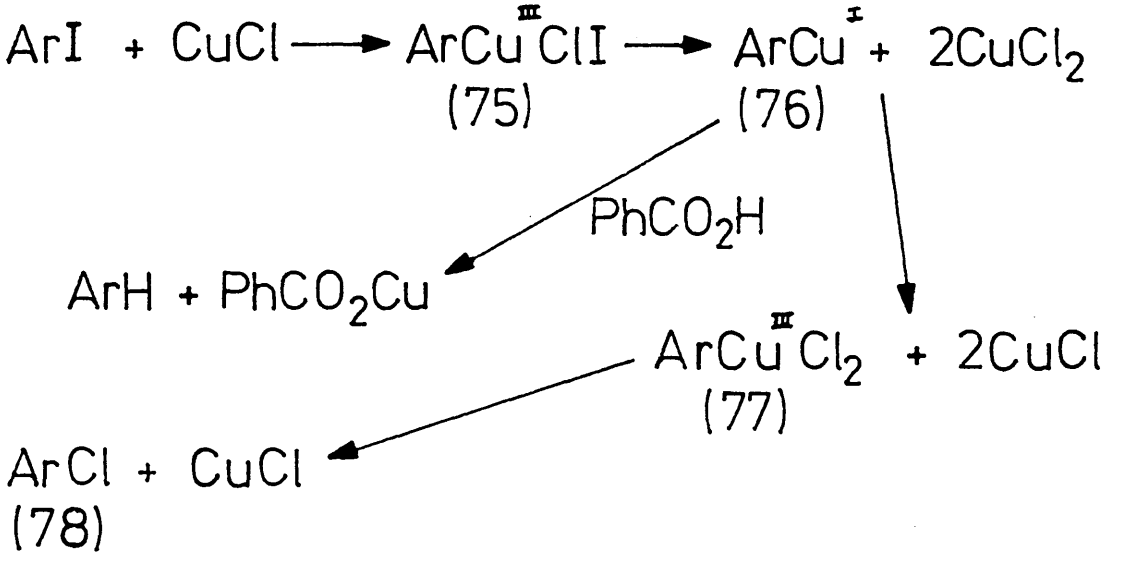
(72)

Kende[54] had prepared and recommended the use of the more stable tris(triphenylphosphine)nickel (0) complex as an Ullmann catalyst, although recent workers[55] have shown that some of these complexes can be prepared *in situ* with zinc powder as the reductant.

The involvement of organocopper intermediates in the exchange reactions of aryl halides with salts of copper (I) has been discussed by Cohen *et al*[56]. It was shown that, in the reaction of *o*-iodo-N,N-dimethylbenzamide (73) with copper (I) chloride or cyanide respectively, in refluxing dimethylformamide (DMF), the addition of benzoic acid resulted in the formation of N,N-dimethylbenzamide (74; X = H) as well as the exchange products (74; X = Cl or CN).



A mechanism was suggested which involved the possible interaction of an arylcopper (III) intermediate as in Scheme 11.

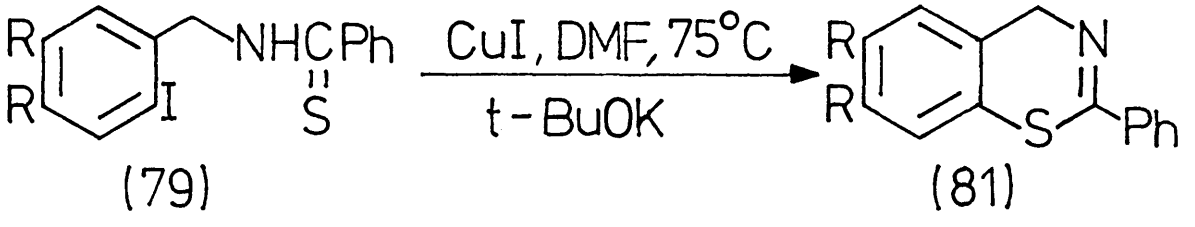


(Scheme 11)

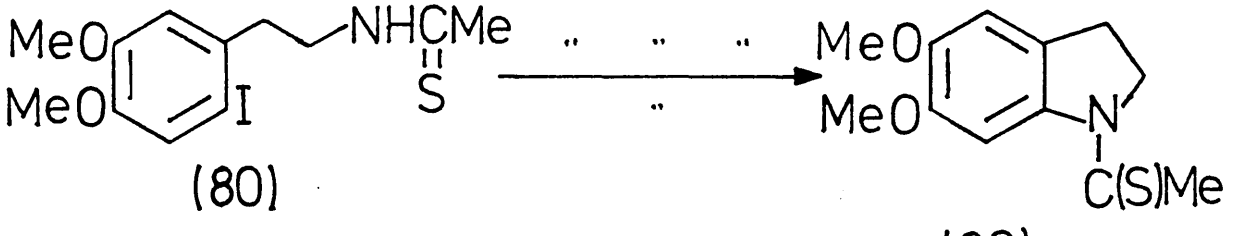
The mechanism involves the oxidative addition of the carbon-halogen bond to copper (I) chloride to form the arylcopper (III) intermediate (75), reduction of which by further copper (I) chloride leads to the aryl-copper (I) species (76). Oxidation of the latter by copper (II) chloride then occurs via a copper (III) intermediate (77) which reductively eliminates copper (I) chloride to give

the product (78). Arylcopper (I) compounds are also known to become protonated by carboxylic acids[57].

Similar studies have been undertaken where the possible involvement of a copper (III) intermediate has been postulated[58,59]. Bowman et al[58] undertook a study of copper (I)-catalysed aromatic nucleophilic substitution reactions with particular reference to the possible involvement of the $S_{RN}1$ mechanism. This study involved the reactions of N-thiobenzoyl-2-iodobenzylamine (79; R=H), the methoxy analogue (79; R=OMe) and its phenylethylamine analogue (80). These compounds underwent cyclisation on treatment with one equivalent of copper (I) iodide in DMF to form the 2-substituted benzo-1,3-thiazine (81; R=H or OMe) and the substituted dihydro-indole (82). It was found that these reactions were not inhibited in the presence of para-dinitrobenzene, a radical scavenger.



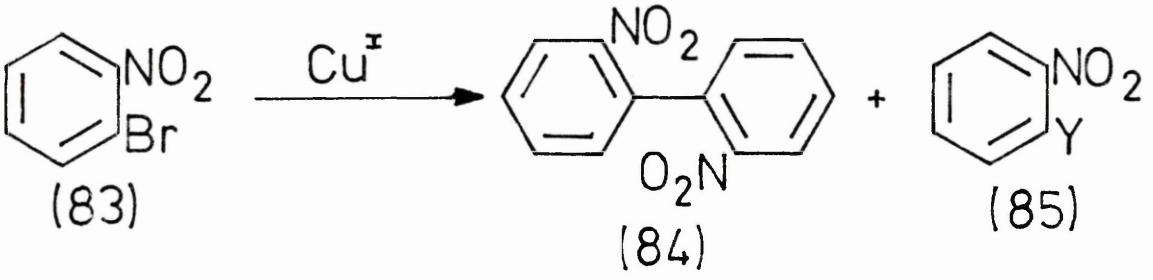
(79) (81)



(80) (82)

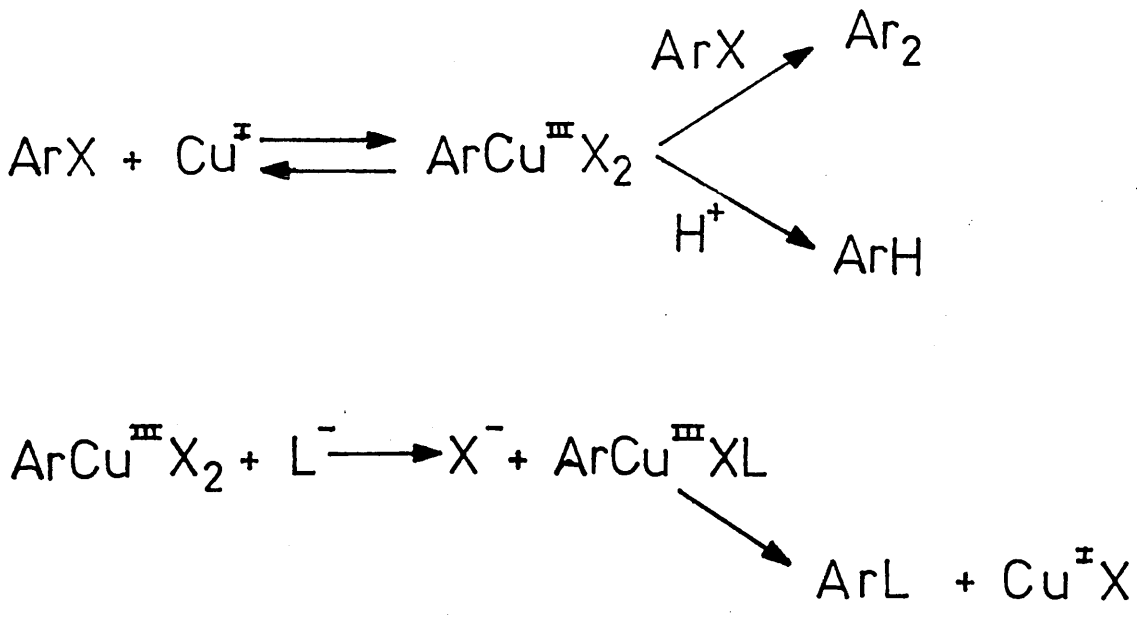
After showing that neither aryl-radicals nor halo-aryl radical-anions are free intermediates in such copper (I) catalysed aromatic substitution reactions, these workers proposed a mechanism similar to that given in Scheme 11 involving oxidative addition of a copper (I) species to the aryl halide, leading to an arylcopper (III) intermediate which then reductively eliminates, giving the product and regenerating the copper (I) catalyst.

Cohen et al[59] reasoned that in the homogenous Ullmann coupling of o-bromonitrobenzene (83), promoted by copper (I) triflate, an aryl-copper (III) intermediate must exist. This intermediate which is reversibly produced by oxidative addition of the carbon-bromine bond to copper (I), is capable of reacting with another aryl bromide to form the biaryl (84) or of becoming protonated by the medium to give (85; Y=H) in a competing process.



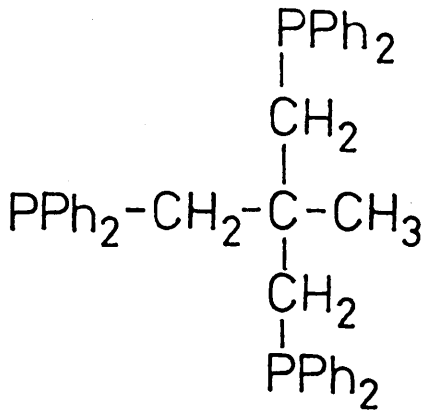
(83) (84) (85)

If these processes are slow, it seems likely that a ligand (L), such as water or ammonia could also displace the bromine from the intermediate to give another copper (III) species which would undergo reductive elimination of copper (I) to produce the protonated phenol or aniline (85; Y=OH or NH_2). This is summarised as in Scheme 12.



(Scheme 12)

Whereas the reduction of copper (II) to copper (I) by phosphorus (III) compounds is well known[60], the related reducion of nickel (II) to nickel (I) in the absence of additional reducing agents is less well documented. However, it is known that nickel (I) complexes of the general formula NiL_nX (L = tertiary phosphine; X = Cl, Br or I) can be generated in the reactions of nickel (II) halides at room temperature, in the presence of sodium borohydride. The same is true when polydentate phosphines replace tertiary phosphines, as, e.g., with 1,1,1-tris(diphenylphosphinomethyl) ethane (86)[61] and tris(2-diphenylphosphinoethyl)amine (87)[62]. In the presence of these ligands, the iodonickel (I) compounds can be obtained even in the absence of external reducing agents.

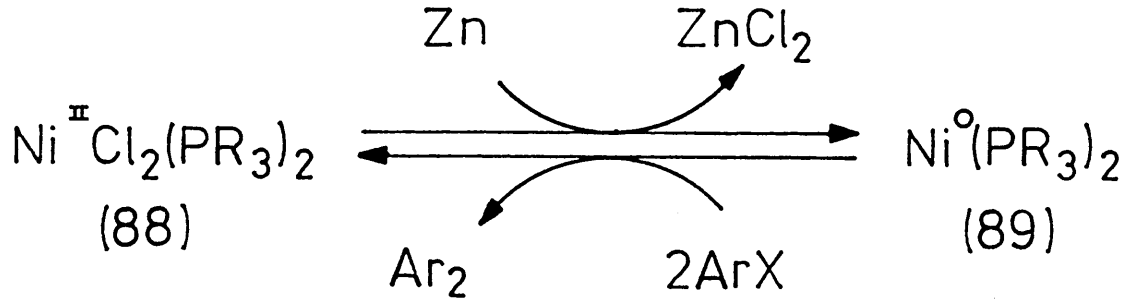


(86)

$(Ph_2PCH_2CH_2)_3N$

(87)

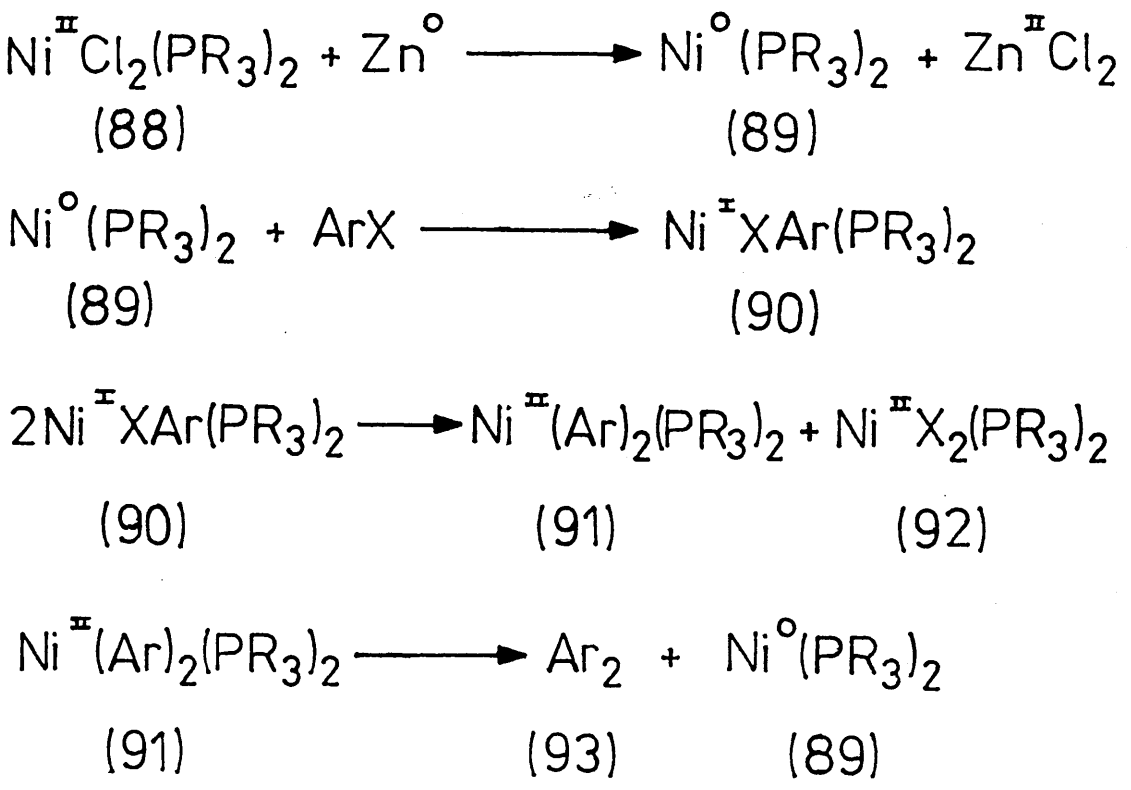
The generation of zerovalent nickel *in situ* from divalent nickel was found to be an effective catalyst for a homo-coupling of aryl halides with zinc powder[63,64]. For this purpose, Takagi *et al*[65,66] used bis(trialkylphosphine)nickel (II) chloride complexes (88) which were reduced *in situ* to the bis(trialkylphosphine)nickel (0) complexes (89) (Scheme 13).



(Scheme 13)

A more detailed mechanism requires that the complex (89) readily reacts with aryl halides to give an oxidative addition product (90). This, in turn, disproportionates giving a nickel (II) halide complex (92) and a diorgano-

nickel (II) species (91) which subsequently yields the biaryl (93), (Scheme 14).



(Scheme 14)

To ensure the continuation of the catalytic cycle, the original nickel (0) complex (89) must be regenerated from the nickel (II) species (92) thus formed and therefore zinc powder in at least a stoichiometric quantity is required.

The use of zinc powder to produce <u>in situ</u> zerovalent nickel complexes has been used to promote the reactions of tertiary phosphines with simple aryl halides, in the presence of nickel (II) bromide, in refluxing ethanol to give arylphosphonium salts[67]. It is also possible that these reactions also involve the intermediacy of aryl-nickel compounds.

$$ArBr + R_3P \xrightarrow[EtOH,\ 80^{\circ}C]{Ni^{II}Br_2,\ Zn\ dust} ArP^{+}R_3Br^{-}$$

It has also been reported that the first example of a direct reduction of nickel (II) to nickel (0) in the absence of other reducing agents has been achieved by heating a trialkylphosphite with nickel (II) chloride to give a tetrakis(triethylphosphite) nickel (0) (94)[68] .

$$\left[Ni\{(EtO)_3P\}_4\right] \text{——— (94)}$$

Oxidative addition of aryl halides to nickel (0) and nickel (I) species is now well established[69,70]. Tsou and Kochi[71] investigated the mechanism of an oxidative addition of aromatic halides to nickel (0) complexes. When applied to aromatic halides (ArX), oxidative addition converts a metal complex, such as a zerovalent d^{10} complex (M), to an organometallic adduct (Equation ii).

$$M(d^{10}) + ArX \longrightarrow \begin{matrix} Ar \\ | \\ M(d^{8}) \\ | \\ X \end{matrix} \quad \text{.....(ii)}$$

It has been shown that aryl halides react with the zerovalent nickel complex (95; L = PEt_3), to give two principal products;

(a) the trans-arylnickel (II) oxidative adduct (96; L = PEt_3; X = Br or I) and (b) the paramagnetic d^9 nickel (I) species (97; L = PEt_3; X = Br or I),(Equation iii).

$$\underset{(95)}{Ni^{0}L_4} + ArX \longrightarrow \underset{(96)}{ArNi^{II}XL_2} + \underset{(97)}{XNi^{I}L_3} \quad \text{.....(iii)}$$

Also noted was the ease with which the nickel (I) species is readily prepared by the synproportionation of nickel (II) and nickel (0) complexes, (Equation iv).

$$Ni^{0}L_4 + X_2Ni^{II}L_2 \longrightarrow 2XNi^{I}L_3 \quad \text{.....(iv)}$$

The reverse of this reaction is easily achieved by promoting the disproportionation of nickel (I) by exposure to carbon monoxide, (Equation v).

$$2XNi^{I}L_3 + 2CO \longrightarrow Ni^{0}(CO)_2L_2 + X_2Ni^{II}L_2 + 2L \quad \text{.....(v)}$$

In cases where the nickel (0) complex (95) is largely converted to the nickel (I) species (97), the major product arising from the reaction with the aryl halide is the corresponding arene (98), which is derived from the aryl radical formed by halogen atom transfer to the nickel (0) complex (Equation vi). Aryl radicals are known to abstract hydrogen atoms from solvents (SH), (Equation vii).

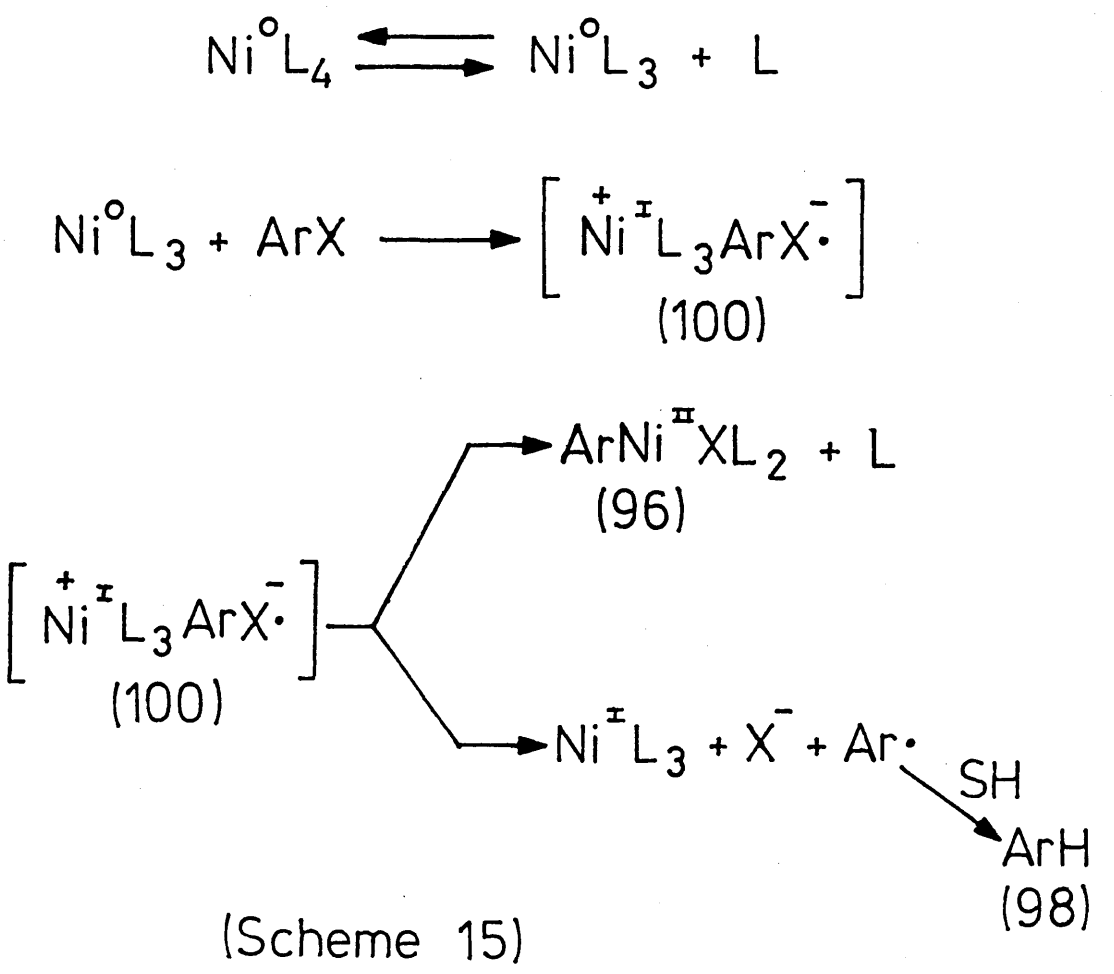
$$Ni^{0}L_4 + ArX \xrightarrow{-L} XNi^{I}L_3 + Ar\cdot \quad \text{.....(vi)}$$

$$Ar\cdot + SH \longrightarrow \underset{(98)}{ArH} + S\cdot \text{ etc} \quad \text{.....(vii)}$$

If an excess of aryl halide is present then a further possibility arises; i.e., the nickel (I) species may be converted into the dihalonickel (II) complex (99) by halogen abstraction, again with the formation of aryl radicals, (Equation viii).

$$\underset{(x's)}{XNi^{I}L_3 + ArX} \longrightarrow \underset{(99)}{X_2Ni^{II}L_2} + Ar\cdot \text{ etc} \quad \text{.....(viii)}$$

Having considered all the factors affecting the formation of nickel (I) and nickel (II) species, including the nature of (a) the aryl halide,(b) the solvent, (c) the effect of polar substituents in the aryl halide, (d) the phosphine and, (e) the effects of potential inhibitors, e.g., radical scavengers, a mechanism was proposed which accounted for all of the products formed (Scheme 15).



(Scheme 15)

The scheme describes the formation of the coordinately unsaturated nickel (0) equilibrium product, which is followed by the rate-determining electron transfer step, which affords the ion-pair intermediate (100). This then collapses yielding either the oxidative addition product (96) or the competitive diffusion product [the arene (98)].

Organometallic compounds of nickel (III) (d^7), involving σ-metal-carbon bonds have been postulated as intermediates in various reactions[72], but only a few compounds of this kind have been isolated[73]. The formation of arylphosphonium salts from nickel (III) and nickel (II) intermediates is known[74,75]. Tsou and Kochi[75] have described a variety of

trans-arylnickel (II) complexes of type (101), which were found to yield only biaryls on treatment with aryl halides.

$$ArNiX(PEt_3)_2$$
(101)

Biaryl formation was shown to involve a radical chain process in which paramagnetic nickel (I) and arylnickel (III) species are the reactive intermediates, (Scheme 16).

$$Ni^{I}X + ArX \longrightarrow ArNi^{III}X_2$$
(102) (103)

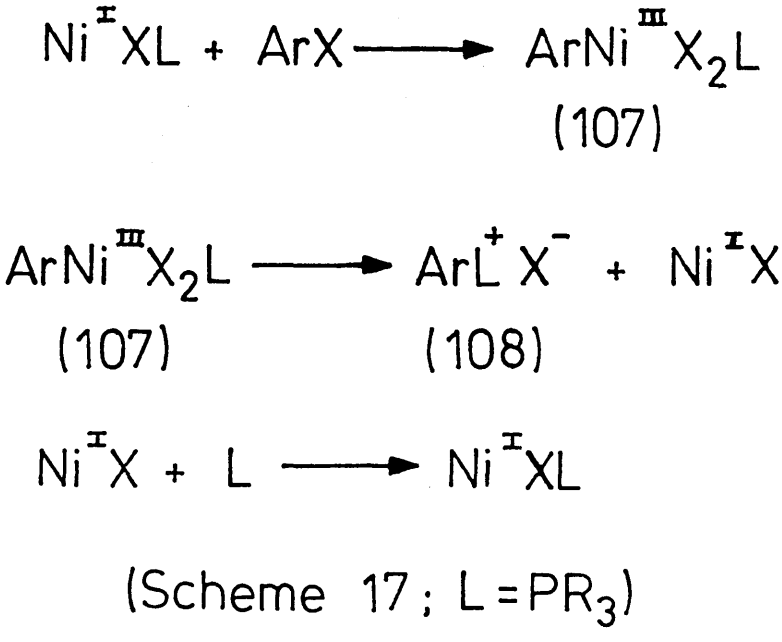
$$ArNi^{III}X_2 + ArNi^{II}X \longrightarrow Ni^{II}X_2 + Ar-Ni^{III}(Ar)X$$
(103) (104) (105)

$$Ar-Ni^{III}(Ar)X \longrightarrow Ar_2 + Ni^{I}X \quad \text{etc}$$
(105) (106) (102)

(Scheme 16)

The propagation step includes the oxidative addition of ArX to the nickel (I) complex (102) to produce the reactive arylnickel (III) species (103), which undergoes aryl transfer with the nickel (II) complex (104) to afford the diarylnickel (III) intermediate (105), followed by reductive elimination of the biaryl (106) and regeneration of the nickel (I) catalyst (102).

These authors have also postulated an alternative mechanism leading to the formation of arylphosphonium salts, (Scheme 17).

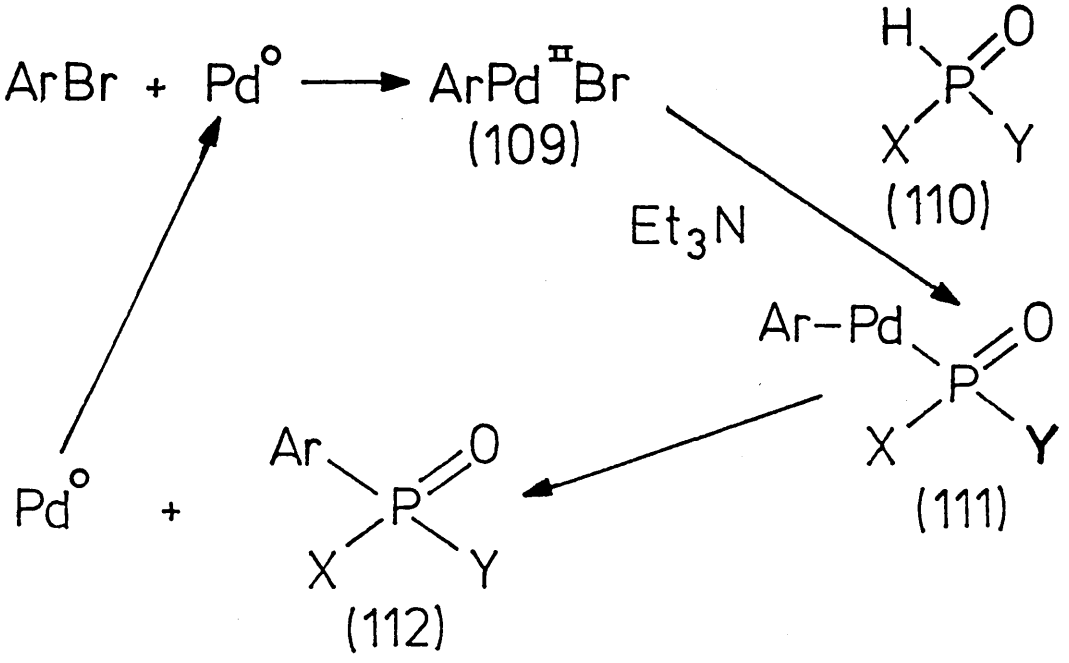


(Scheme 17 ; L = PR_3)

Again generation of a nickel (III) intermediate (107) is afforded by the oxidative addition of ArX to the nickel (I) species. The arylphosphonium salt (108) arises by reductive elimination from the metastable arylnickel (III) complex (107). The ejected nickel (I) species then accommodates another phosphine ligand so that the cycle can continue. Tsou and Kochi showed that independent generation of an aryl(phosphine)nickel (III) complex (107) by either electrochemical or chemical oxidation of an arylnickel (II) halide affords excellent yields of arylphosphonium salts[76]. Their workers also demonstrated that solvent effects play a major role in deciding the outcome of the reaction between an aryl halide and a nickel (0) phosphine complex. When hydrocarbon solvents are used, the product

is always the biaryl, whilst phosphonium salts dominate when polar solvents are employed (e.g. EtOH).

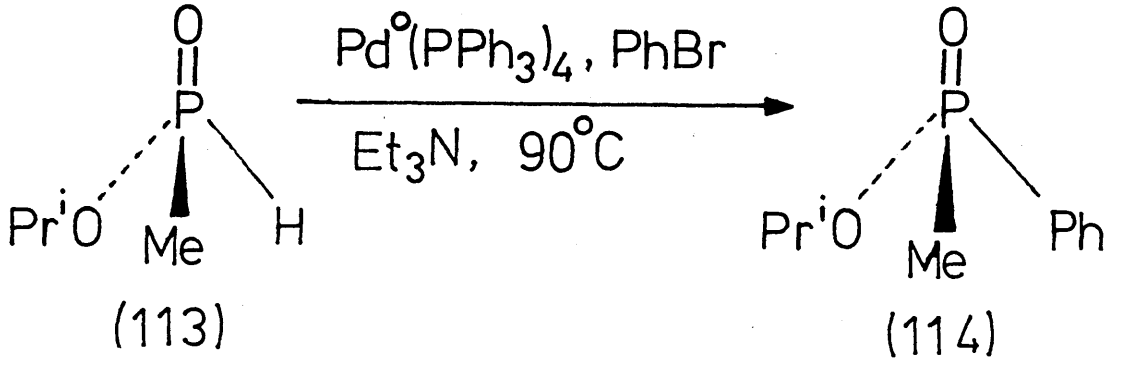
A recent paper by Xu and Zhang[77] provides another example of the oxidative addition/reductive elimination pathway, involving the palladium-catalysed formation of carbon-phosphorus bonds from aryl halides. The proposed mechanism is as follows, (Scheme 18).



(Scheme 18; X,Y= R,Ph or OR)

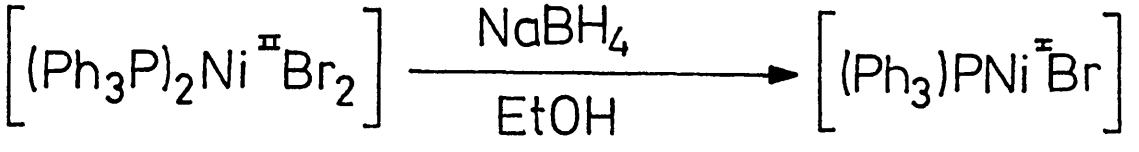
The palladium (0) species undergoes oxidative addition with the aryl bromide to give the arylpalladium (II) complex (109). Attack of the phosphorus nucleophile (110) at the aryl palladium complex in the presence of triethylamine results in the elimination of hydrogen bromide to give the palladium (II) intermediate (111) which then undergoes reductive elimination to afford the final product (112) and

regenerate the Pd° catalyst. The reaction of (R)-(+)-isopropylmethylphosphinate (113) with bromobenzene in the presence of tetrakis(triphenylphosphine)palladium (0) catalyst and triethylamine yielded (S)-(-)-isopropylmethyl-phenylphosphinate (114). This clearly demonstrates that the palladium-catalysed formation of phosphorus-arylcarbon bonds occurs with complete retention of configuration at the chiral phosphorus atom.



(113) (114)

In the nickel (II) catalysed reactions of o-halogeno Schiff's bases with tertiary phosphines, Allen et al[41] have observed that the rate of phosphonium salt formation increases rapidly when the Schiff's bases are treated with the nickel (I) complex (116) [prepared by the reduction of the nickel (II) complex (115) with sodium borohydride in ethanol[78]].



(115) (116)

This result lends support to their suggestion of an *in situ* reduction of the metal from the +2 oxidation state, in which intramolecular co-ordination involving the imino nitrogen of the Schiff's base has a key role in stabilising the lower oxidation state and in promoting the subsequent reactions leading to phosphonium salt formation.

1.5 AIMS AND OBJECTIVES

In order to shed further light on the template-assisted formation of arylphosphonium salts, the following study was proposed:-

(i) The synthesis of a range of potential template o-donor substituted aryl halides and a study of their metal ion-catalysed reactions with tertiary phosphines in order to define more clearly the factors responsible for the selectivity of such reactions in terms of the nature of the potential co-ordinating template centre in the substrate, and the nature of the metal ion catalyst.

(ii) Investigation of the kinetics of such reactions in order to establish the dependence of the rate on the nature and concentration of the aryl halide, the phosphine and the metal ion catalyst, and hence to draw conclusions concerning the likely mechanism of the reactions.

(iii) In the light of the results of the above kinetic study, to devise experiments to test proposed mechanisms. It is likely that such studies would involve the preparation of metal complexes of phosphines in which the metal ion is in a lower oxidation state than normal, and a study of their interactions with aryl halide substrates.

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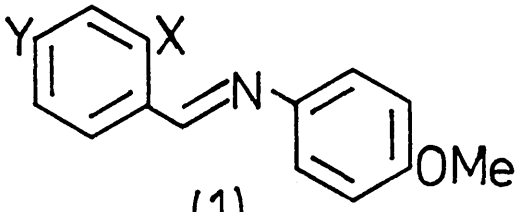
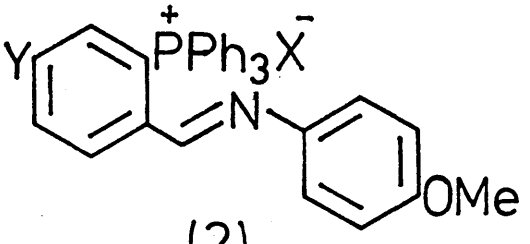
CHAPTER 2: DESIGNS AND SYNTHESIS OF POTENTIAL TEMPLATE SYSTEMS

2.1 INTRODUCTION

Earlier work by Price[1], and later by Allen[2] has shown that many factors are responsible for the selectivity of metal-ion catalysed template reactions. The very critical nature of the donor atom and its position with respect to the ortho-halogen for the promotion of a template-assisted replacement reaction has been illustrated by studies of the reactivity of a number of related systems[2]. The Schiff's bases (1; Y = H or Cl, X = Cl, Br or I) undergo conversion to the phosphonium salts (2; Y = H or Cl, X = Cl, Br or I) on prolonged refluxing in dry ethanol with triphenylphosphine, in the presence of nickel (II) bromide.

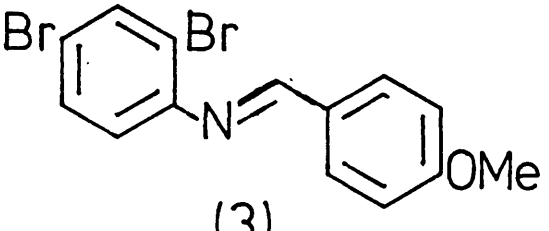


(1)



(2)

However, the Schiff's base systems (3) and (4) fail to undergo conversion to the respective phosphonium salts. Neither system, apparently, has the ability to be involved in an appropriate mode of metal coordination to promote the reactions leading to the replacement of the ortho-halogen atom.



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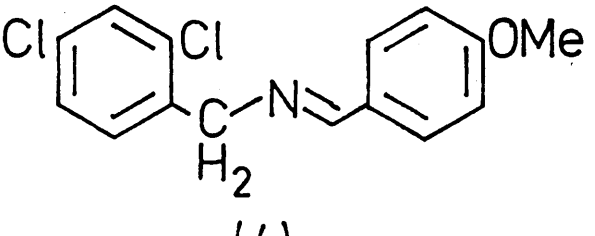
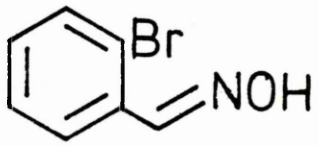


(4)

Other systems which remain unreactive include the oxime (5), the semicarbazone (6) and the o-halogeno-benzylamine (7). The latter group, whilst having a nitrogen atom in the same relative position as in the reactive Schiff's bases (1; Y = H or Cl; X = Cl, Br or I) nevertheless fails to undergo conversion to the related phosphonium salt.



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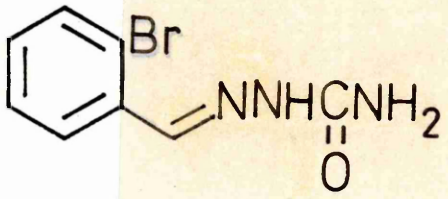


(6)

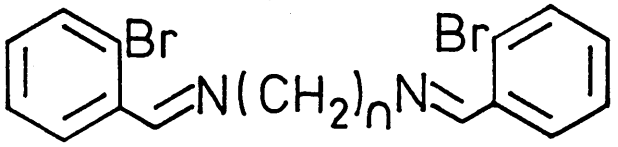
(7)

Clearly, some very subtle coordination and stereo-chemistry is involved in these template reactions. In the following sections the preparation and the reactions of a range of potential new template molecules are discussed.

2.2 SYNTHESIS AND REACTIONS OF SOME BIS-SCHIFF'S BASE TEMPLATES

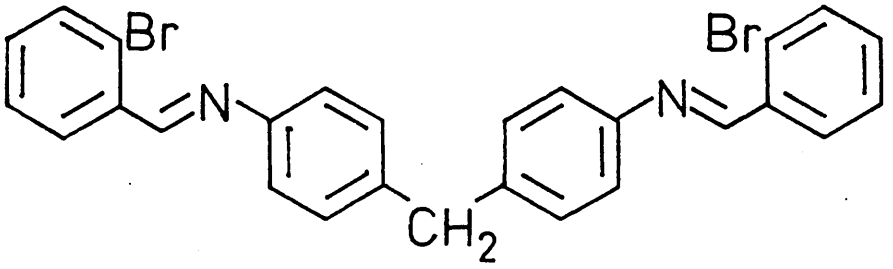
2.2.1 Synthesis

The synthesis of a range of bis-Schiff's bases (8; n = 0,2,3-8,12) was achieved by reacting together the readily available o-bromobenzaldehyde (2 mol equiv.) with the appropriate α-ω diamine (1 mol equiv.) in refluxing ethanol under an inert atmosphere for 1-2 hours.



(8)

Compounds (9), (10) and (11) were prepared using the same conditions, but with replacement of the α-ω diamine by 4,4´-diaminodiphenylmethane, para-phenylene diamine, and 2,2´-diaminobiphenyl, respectively. The products crystallised on cooling and all the yields were greater than 80%.



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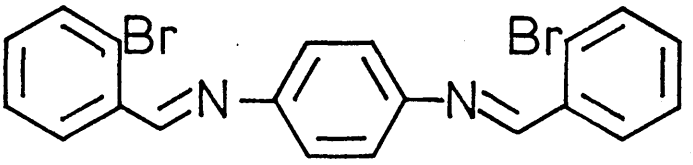

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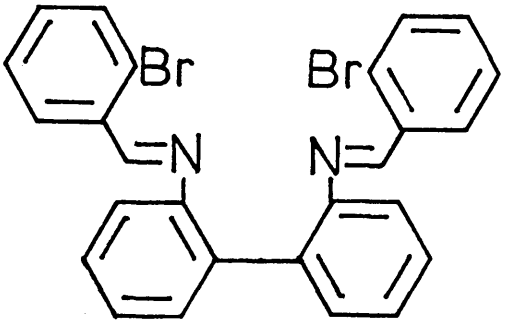
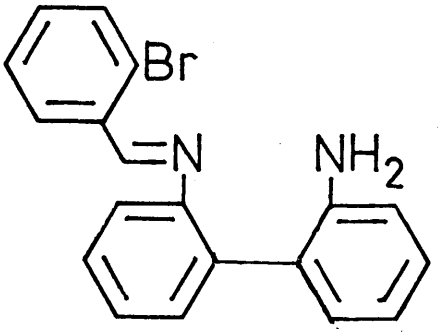


(11)

Characteristic ^{1}H n.m.r. signals were observed for these compounds with the expected imino-proton signal appearing as a sharp singlet at 8.6δ. In the infrared spectra, two or three characteristic bands appear between 1558-1631cm^{-1} for all of the bis-Schiff's bases. These bands are attributed to the Schiff's base moiety (i.e. RC(H)=N-).

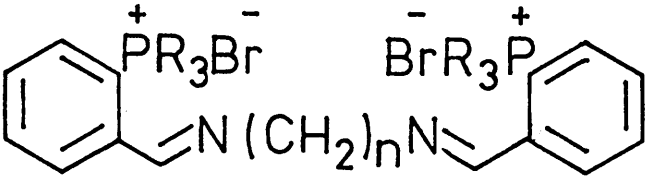
Attempts to synthesis the mono-Schiff's base (12) by altering the molar ratios (i.e. 1:1 mol equiv.) failed, and it is clear that the formation of the bis-product is in some way favoured.



(12)

2.2.2 Reactions

When o-bromoaryl-bis Schiff's bases (8; n = 0, 3-8, 12), (9) and (10) were heated under reflux in ethanol in a nitrogen atmosphere, with either triphenyl- or tributyl-phosphine in the presence of a catalytic amount of nickel (II) bromide, the related bis-phosphonium salts (13; n = 0, 3-8, 12, R = Ph or Bu), (14, R = Ph or Bu) and (15; R = Ph or Bu) were formed.



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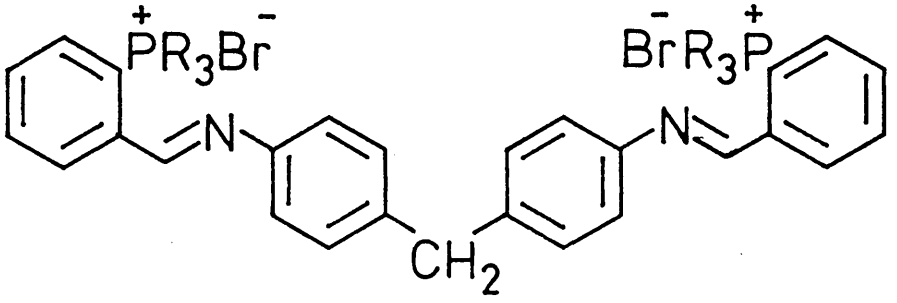

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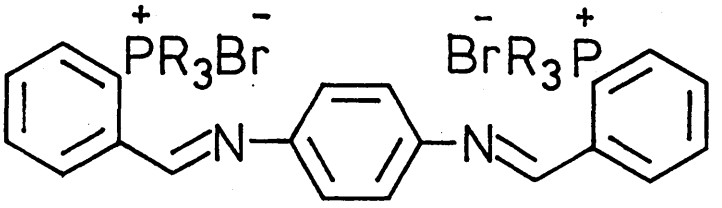
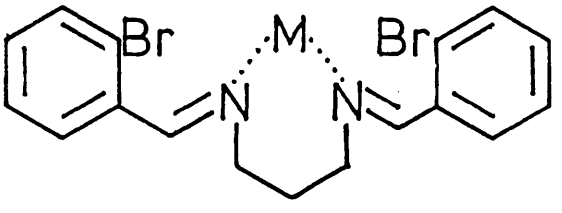


(15)

In contrast, the Schiff's bases (8; n = 2) and (11), both of which have the potential to form five- and seven-membered ring chelate complexes, respectively, with the metal ion, do not undergo the substitution reaction on treatment with a tertiary phosphine in the presence of nickel (II) bromide. Instead, it was found that these substrates undergo hydrolysis to form o-bromobenzaldehyde and the respective diamine. These results imply that when the Schiff's base bears a second donor group which is capable of coordinating with the metal ion, especially when the formation of a chelate complex is possible, then the metal ion is diverted away from its catalytic role in salt formation. The yield of salt derived from the Schiff's base (8; n = 3) was greatly reduced, probably due to the competition between the substitution reaction and the ability of the compound to form a six-membered chelate ring (16; M = metal).



(16)

Valuable information on the introduction of either triphenyl- or tributyl-phosphine was gained from the ^{1}H n.m.r. and infrared spectra of the salts. Integration of ^{1}H n.m.r. spectra confirmed the presence of the bis-phosphonium salt rather than the mono species. The infrared spectra of certain salts (i.e. those containing phenyl groups) exhibited strong bands at 750 cm^{-1} which were not observed in the spectra of the starting bis-Schiff's base substrates.

^{31}P n.m.r. spectra were recorded for the bis-phosphonium salts and all of the spectra exhibited only one signal either between 24-26 ppm (characteristic of the tetra-arylphosphonium salts) or between 33-35 ppm (trialkylarylphosphonium salts).

Great difficulty has arisen in characterising such bis-phosphonium salts by microanalysis, especially in the case of the alkylene-bridged salts (13, n = 3-8, 12). Microanalyses of these compounds, although within acceptable limits for %H and %N, consistently resulted in low %C results. This may be due to either the difficulty in ensuring full combustion of such samples, (thus, e.g., the RMM of (14,R = Ph) is $\sim$1096), or as a result of the hygroscopic nature of the samples. Even the mercuric bromide salts, i.e. $R_4P^+HgBr_3^-$, obtained by treatment of the phosphonium halide with mercuric bromide ($HgBr_2$) in ethanol, (based on the preparation reported by Deacon et al[3]), failed to give acceptable microanalytical data.

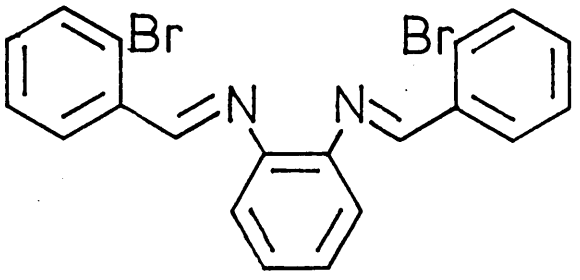
2.3 SYNTHESIS AND REACTIONS OF ALTERNATIVE TEMPLATE SYSTEMS

2.3.1 Nitrogen Donors

Other potential template systems having a nitrogen donor atom in the same relative position as in the reactive Schiff's bases (1; Y = H or Cl; X = Cl, Br or I), and conforming to Price's type II and type III classification of aryl halides[1] have been synthesised and their reactions with tertiary phosphines in the presence of metal ions studied.

2.3.1 (A) Synthesis

During the course of the previous study on bis-Schiff's bases, the attempted preparation of the bis-imine (17) from the reaction of o-bromobenzaldehyde (2 moles) and o-phenylenediamine (1 mole) in ethanol, unexpectedly gave rise to the pale yellow 1,2-disubstituted benzimidazole (18)[4]. The ^{1}H n.m.r. spectrum was not consistent with the assumed structure (17), the expected signal at δ=ca 8.5 ppm, characteristic of an aldimine, being absent. In contrast, the spectrum displayed a sharp singlet at δ=5.3 ppm, suggesting the presence of a benzylic substituent.



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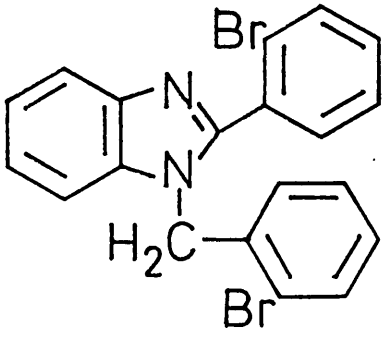

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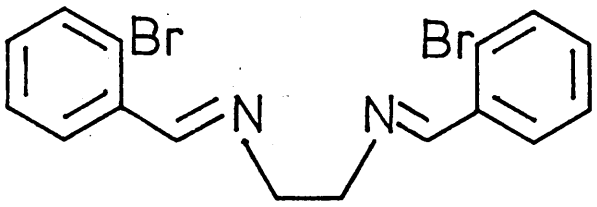
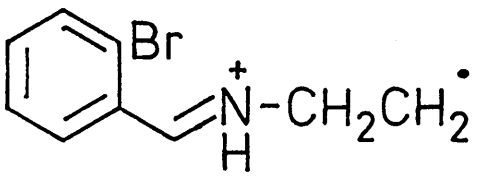


(19)

The mass spectrum revealed an apparent prominent molecular ion at m/e 442, as required by the bis-Schiff's base (17). However, the fragmentation pattern differed markedly from that of the related bis-imine (19), which exhibited only a low intensity molecular ion at m/e 394. The base peak in the spectrum corresponds to the fragment (20) (m/e 211), arising from the elimination of the stable neutral fragment (21) from the molecular ion. The mass spectra of both compounds, however, exhibited a signal at m/e 169, which corresponds to the o-bromobenzyl fragment (22). The origin of such a fragment (22) in the spectrum of the bis-imine (19) is not obvious and is possibly the result of a rearrangement process taking place.



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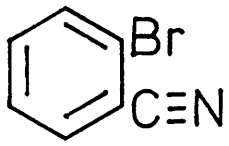

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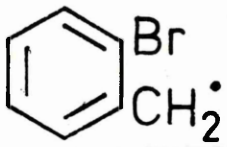
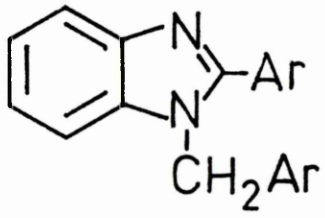


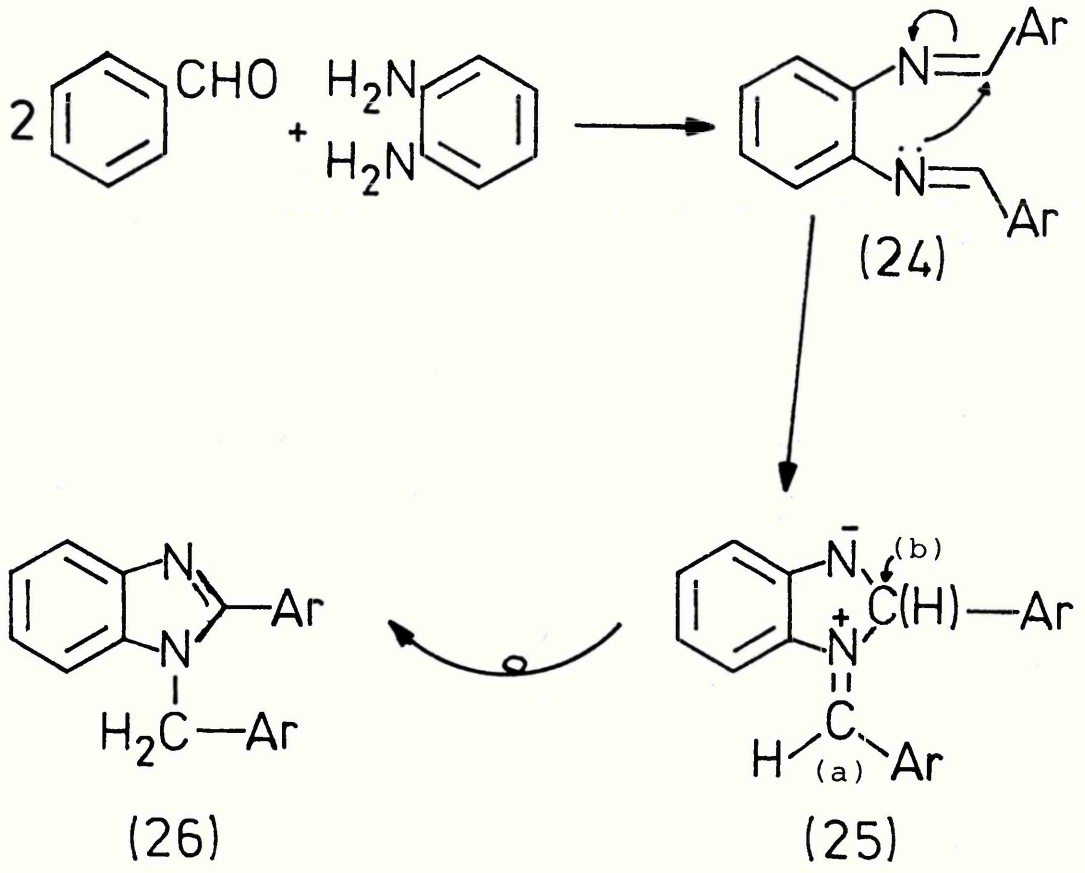
(22)

A search of the literature revealed that the reactions of o-phenylenediamine with aromatic aldehydes result in the formation of the benzimidazoles (23) via an intramolecular redox process[5,6], and thus the reaction of o-bromobenzaldehyde and o-phenylenediamine has given rise to the o-bromophenyl derivative (18), a structure which is consistent with the observed ^{1}H n.m.r., mass spectra and microanalytical data.



(23)

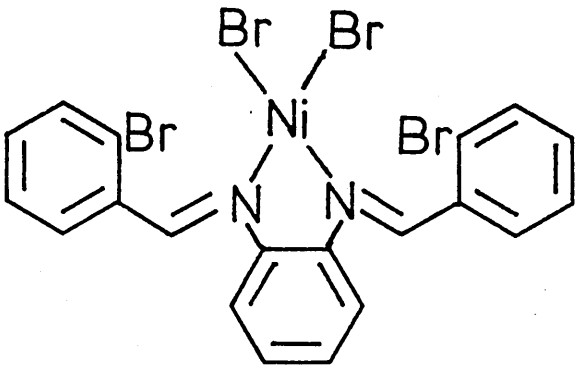
Although the authors[6] failed to speculate on a detailed mechanism, it is thought that the formation of the benzimidazoles might initially involve the formation of the transient bis-Schiff's base (24), followed by an intermolecular addition, producing the immonium ion intermediate (25) which can then enter an oxidative addition/reductive elimination pathway at the carbon sites ((a) and (b)), thus yielding the 1,2-disubstituted benzimidazole product (26), as outlined in Scheme 1.



(Scheme 1)

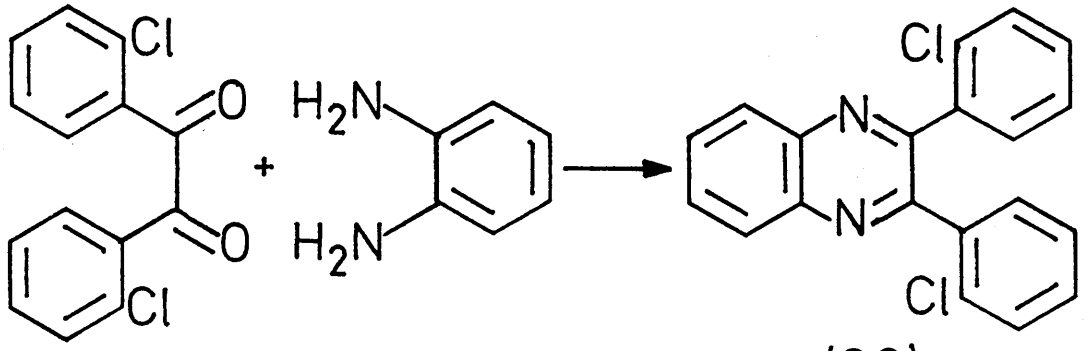
The appearance of the benzylic protons in the benzimidazole (26) acts as a characteristic marker in the ^{1}H n.m.r. spectrum.

The attempted preparation of the bis-Schiff's base (17) by the "thermodynamic template effect" involving the sequestration of the bis-Schiff's base (17) in a five membered chelate ring using nickel (II) ions, failed. The expected product (28) was not obtained.



(28)

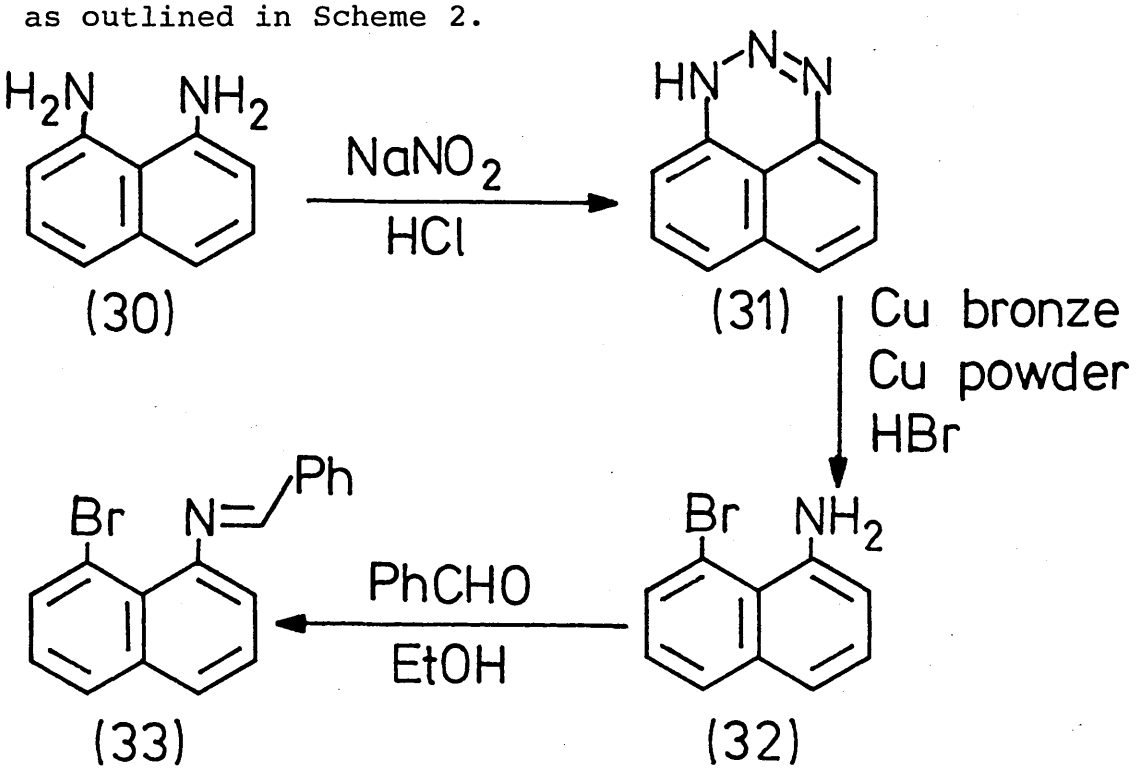
The synthesis of the 1,2-disubstituted quinoxaline (29) was achieved by heating together equimolar amounts of 2,2´-dichlorodibenzoyl and o-phenylenediamine in ethanol. The product crystallised on cooling in quantitative yield.



(29)

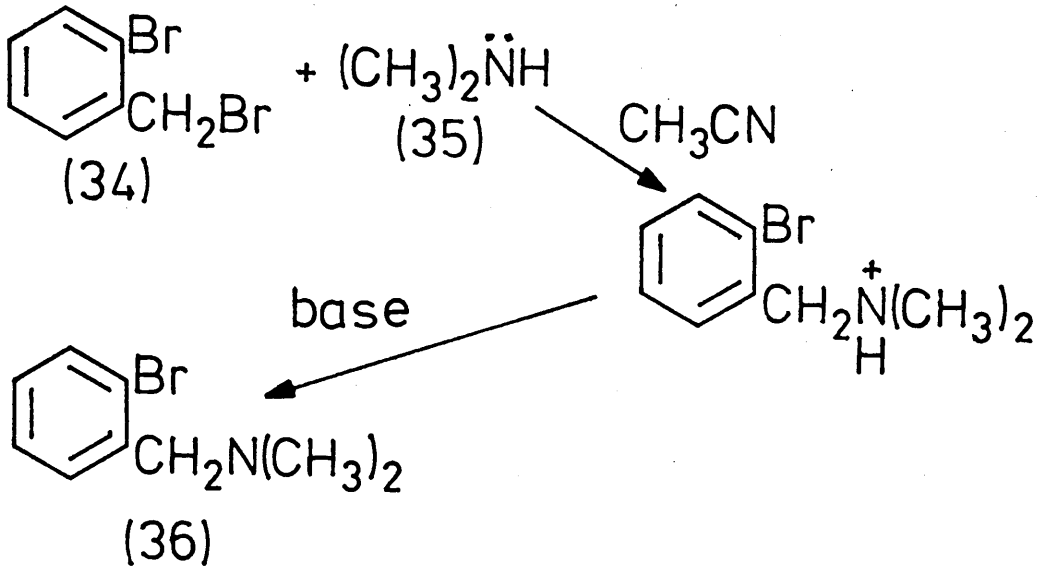
The preparation of the bromonaphthalene derivative (32) involved the diazotization of the diaminonaphthalene compound (30) to produce the intermediate azimino compound (31). This was then dried and heated under reflux in hydrobromic acid in the presence of heat-treated copper bronze and copper powder. From this copper-assisted substitution reaction, the resulting bromonaphthalene (32) was recovered and recrystallised from petrol/ether as described by Fieser and Seligman[7]. The synthesis of the imine (33) was completed by the reaction of equimolar

amounts of the bromonaphthalene (32) with benzaldehyde in ethanol to yield the 8-bromo-1-iminonaphthalene (33), as outlined in Scheme 2.

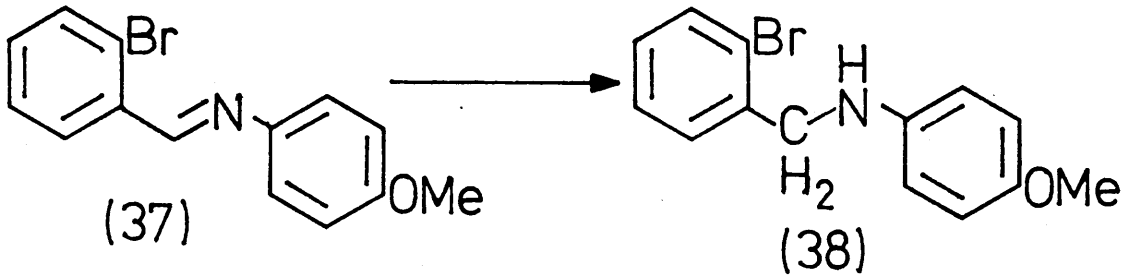


(Scheme 2)

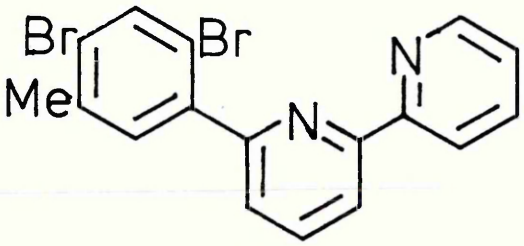
The o-bromobenzylamine (36) was synthesised by treating the readily available o-bromobenzylbromide (34) with an excess of dimethylamine (35) [produced *in situ* from methylamine hydrochloride and sodium carbonate] at room temperature in acetonitrite.



The o-bromobenzylamine (38) was prepared by the reduction of the Schiff's base (37) [isolated from the condensation reaction using equimolar amounts of o-bromobenzaldehyde with p-anisidine in ethanol][8] using an excess of sodium borohydride in ethanol.



The aryl halide (39) having a dipyridyl side chain, which according to Price's classification of aryl halide substrates[1], is a type III system (40; X = Halogen, D = donor atom), (i.e. it possesses two donor centres which could interact with a metal ion) was supplied by I.C.I., Organics Division, Blakely, Manchester.



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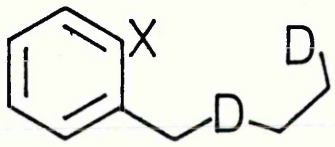
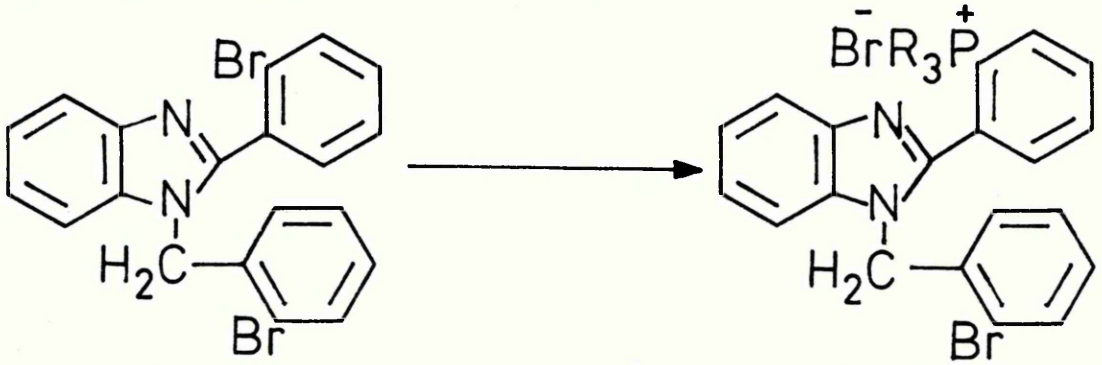


(40)

2.3.1 (B) Reactions of Potential Templates with Phosphines

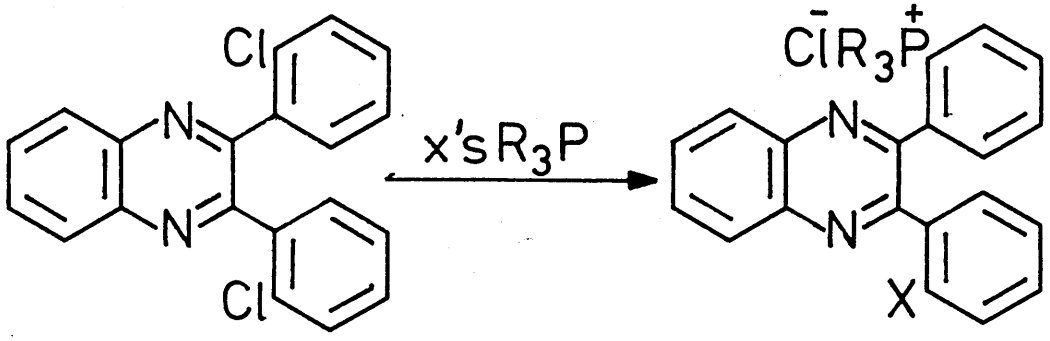
The reactions of the 1,2-disubstituted benzimidazole (18) in refluxing ethanol with triphenyl- and tributyl-phosphine in the presence of nickel (II) bromide gave the respective phosphonium salts (41; R = Ph or Bu) in yields of 54 (R = Ph) and 46% (R = Bu).



(18) (41)

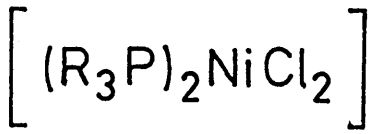
The substitution reaction was not catalysed by any other transition metal salt (e.g. Copper or Cobalt) and the structure of the yellow crystalline salt (41; R = Ph) was proved by X-ray analysis (see Chapter 4).

On heating the 1,2-disubstituted quinoxaline (29) in ethanol with excess triphenylphosphine or tributyl-phosphine in the presence of only nickel (II) bromide, the colourless phosphonium salts (42; R = Ph or Bu, X = $P^{+}R_3C\bar{l}$ or Cl) were produced in good yields.



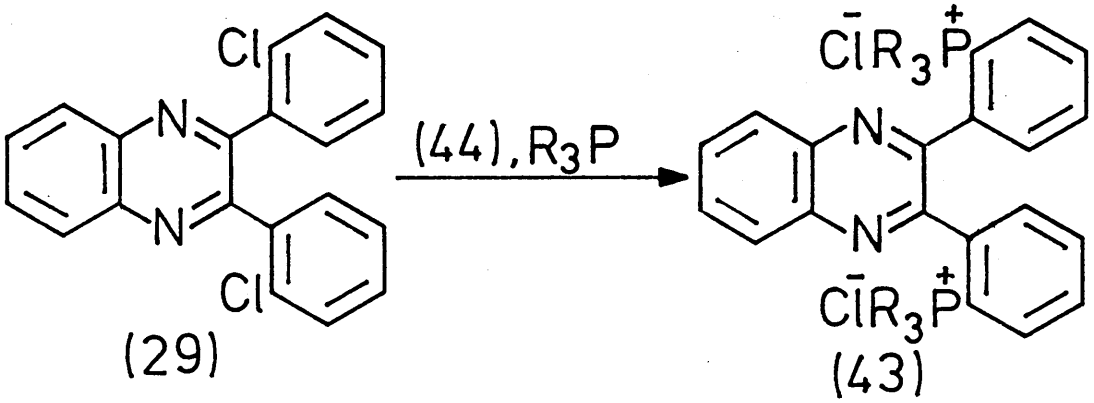
(29) (42)

The ^{31}P n.m.r. spectra of both products exhibited two signals (of differing intensities) with chemical shifts of 26.7 and 25.2 ppm (R = Ph; in a 3:1 ratio) and 34.2 and 32.6 ppm (R = Bu; in a 3:4 ratio), respectively. It is likely that these signals arise from a mixture of mono- and di-phosphonium salts since the quinoxaline (29) contains two possible reaction sites where the substitution reaction could occur. Integration of the ^{1}H n.m.r. spectra of these products lent support to this suggestion. It was not possible to separate the mixed salts into the mono- and di-species. Isolation of the diphosphonium salt (43; R = Ph or Bu) was only possible when the quinoxaline was heated in ethanol with the preformed nickel (II) phosphine complex (44; R = Ph and Bu) and an additional quantity of the free phosphine (1 mol equiv.). The latter complexes were prepared by mixing together nickel (II) chloride (1 mol equiv.), dissolved in hot ethanol with the appropriate tertiary phosphine (2.2 mol equiv.), dissolved in ethanoic acid [9].



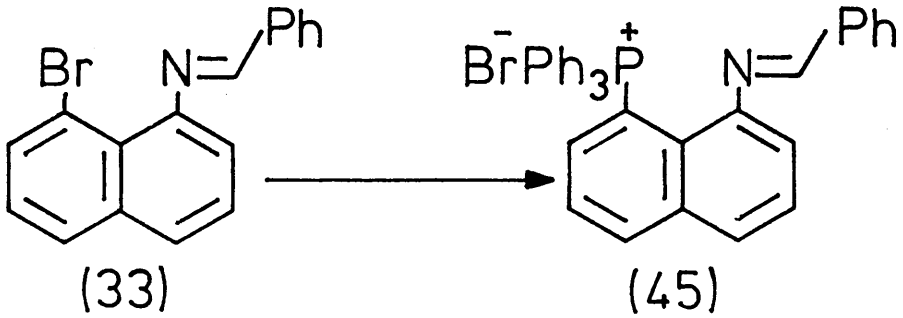
(44)

The reaction of equimolar amounts of the quinoxaline (29) with the preformed nickel (II) complexes (44; R = Ph or Bu), but excluding the extra mole of tertiary phosphine, led to the mixture of the mono- and di-phosphonium salts.



(29) (43)

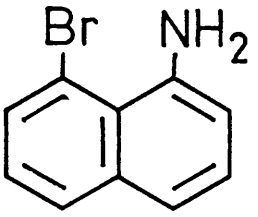
The reaction of the 8-bromo-1-iminonaphthalene (33) with triphenylphosphine gave the phosphonium salt (45) when heated under reflux in ethanol with nickel (II) bromide. Copper (II) acetate failed to catalyse the reaction.



(33) (45)

In contrast, the precursor to the imino-naphthalene (33), the bromo-naphthylamine (32), which fits into Price's

classification as an example of a type II halide (46; X = Cl, Br or I; D = donor atom) fails to undergo conversion to a phosphonium salt in the presence of a tertiary phosphine and nickel (II) bromide, under the usual conditions.



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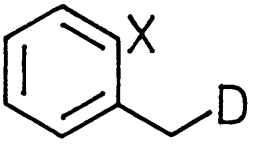
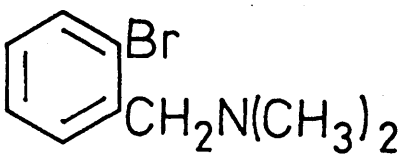
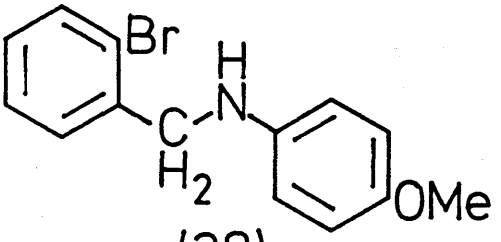


(46)

When the benzylamines (36) and (38), (both of which are type II donors in Price's classification), were treated with tertiary phosphines in the presence of <u>either</u> nickel (II) bromide of copper (II) acetate, neither underwent the substitution reaction to produce the related phosphonium salts.



(36)

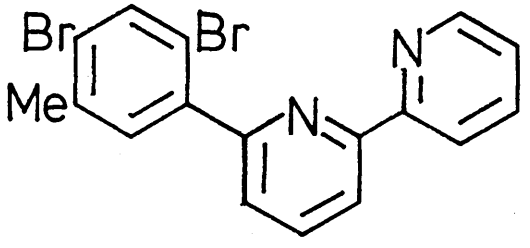


(38)

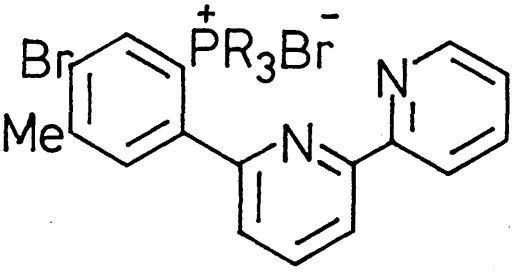
Clearly, the nature of the donor atom is most important in this type of template reaction. Thus, although the donor atom occupies the same relative position as in reactive substrates, i.e. certain types of Schiff's bases[10], it must also be unsaturated, i.e. possess some form of Π-acceptor character.

The halide (39) is the only example discussed in this section in which two donor centres are present in the aryl

halide. Unlike the previous examples, the reactions of this substrate with triphenyl- or tributyl-phosphine were found to be catalysed by both nickel (II) bromide and copper (II) acetate leading to the formation of the phosphonium salts (47; R = Ph or Bu) in good yields. ^{31}P n.m.r. studies indicated that the products were free of phosphorus-containing impurities (e.g. $R_3P=0$ or R_3P), the salts having ^{31}P chemical shifts of 23.8 ppm (R = Ph) and 32.6 ppm (R = Bu), respectively. ^{1}H n.m.r. spectra were also consistent with the formation of a mono-phosphonium salt, thus implying that regiospecific replacement of the halogen ortho to the donor group had occured, the para halogen remaining unaffected. Proof of the structures of these compounds relies on microanalytical data, ^{1}H and ^{31}P n.m.r. studies, and the results of an X-ray crystallographic study of (47; R = Ph) (see Chapter 4).



(39)



(47)

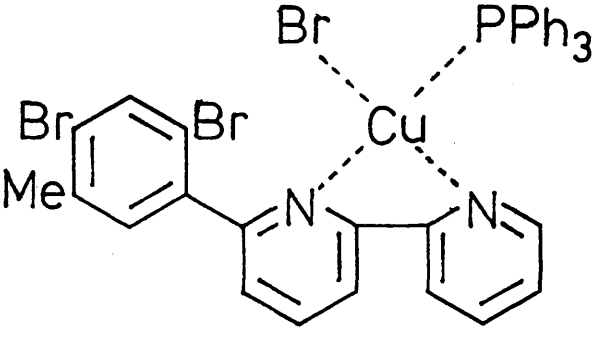
The reactions of the halide (39) with the preformed copper (I) bromide complex (48) were also studied. This complex was prepared by the reaction of an equimolar amount of triphenylphosphine with copper (I) bromide in ethanol[11].

$$Cu^{I}Br + Ph_3P \xrightarrow{EtOH} \left[Ph_3PCu^{I}Br\right]_4$$

(48)

The reaction of the halide (39) (1 mol equiv.) with the preformed copper (I) complex (48) (1 mol equiv.), together with triphenylphosphine (1 mol equiv.), gave the corresponding colourless phosphonium salt (47; R = Ph) in good yield (ca 60%).

When the same reaction was carried out using equimolar amounts of the substrate (39) and the catalyst (48), but excluding the additional mole of triphenylphosphine, a red solution resulted. On standing overnight, orange-red crystals formed. On the basis of microanalytical data, and the ^{31}P nmr spectrum which exhibited a signal at $\delta = -4.96$ ppm (implying the presence of a PPh_3 substituent), it is proposed that this product could be a copper (I) bromide complex of the halide (39) together with 1 mole of triphenylphosphine of the type (49). Related complexes of bipyridyl ligands have been prepared by Jardine[11].

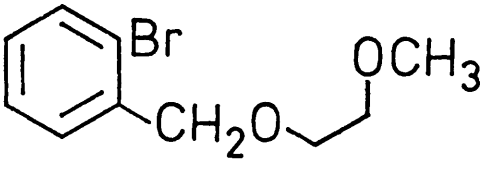


(49)

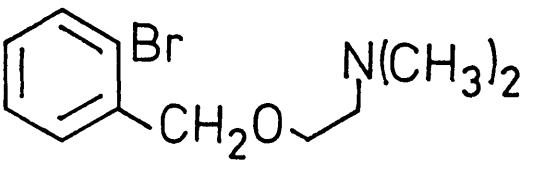
On heating an equimolar mixture of the orange-red complex (49) and triphenylphosphine in ethanol, it was found that at higher temperatures (60°C), competition for the copper nucleus takes place between the bidentate bipyridyl ligand (39) and the tertiary phosphine. The loss of the orange-red colour at higher temperatures suggests that the copper-phosphorus coordination is predominant. On cooling the solution, the orange-red colour reappeared, indicating that the copper-bipyridyl complex (49) had reformed.

2.3.2 Donors Other Than Nitrogen

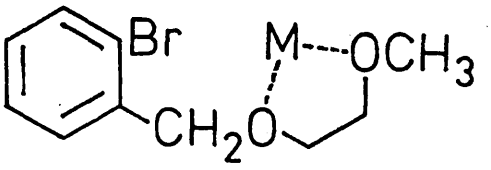
It has already been shown[2] that replacement of the nitrogen donor by oxygen as in the ethers (50) and (51) does not promote the substitution reactions to produce the corresponding phosphonium salts. It is clear that these two compounds belong to the type III aryl halide classification[1] and the most probable reason why they do not undergo the substitution reaction is because of the possible formation of five membered chelate complexes with the transition metal catalyst (52) and (53) (M = nickel or copper). It can also be added that the oxygen atoms



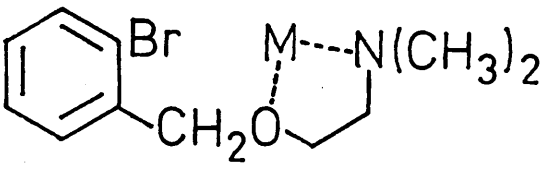
(50)



(51)



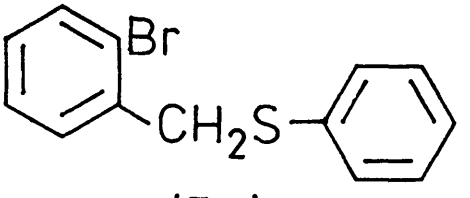
(52)



(53)

in these two examples are completely different in their donor properties from the nitrogen donor atoms found in examples of reactive Schiff's base templates[10].

Other donors, e.g., sulphur, as in the thioether (54), have also been investigated, but again such compounds seem to be inert on prolonged heating in ethanol with triphenylphosphine, in the presence of a transition metal (II) ion, e.g., nickel (II) or copper (II).



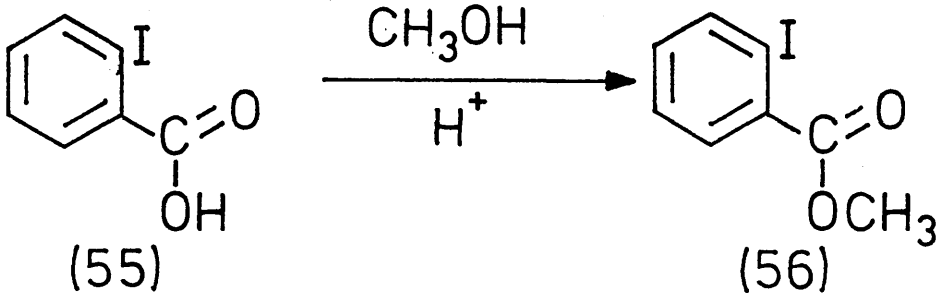
(54)

In the next section a range of oxygen donor molecules have been synthesised and their reactions with tertiary phosphines and transition metal catalysts have been investigated.

2.3.2 (A) Synthesis

The synthesis of the o-iodobenzoate ester (56) was carried out by heating the commercially available o-iodobenzoic acid (55) in absolute methanol containing

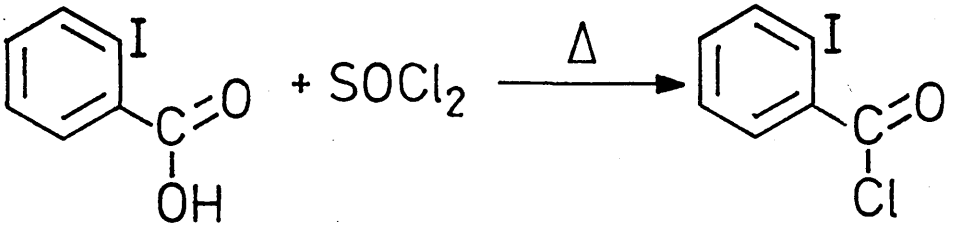
sulphuric acid as the catalyst[12].



(55) (56)

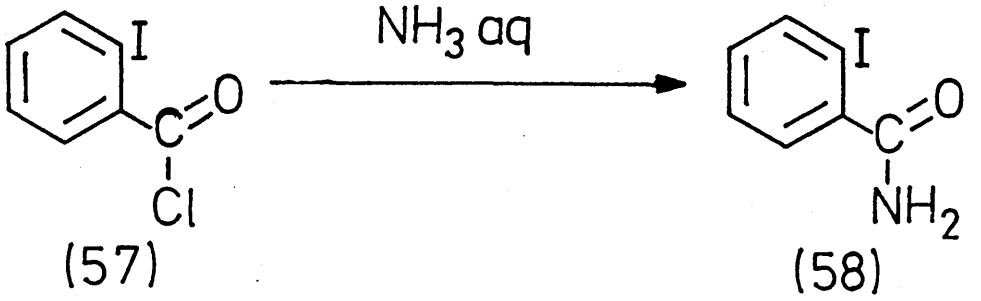
The product was purified by vacuum distillation to give the ester in good yield.

The preparation of the o-iodobenzamide (58) was carried out via the intermediate acid chloride (57). This was made by heating o-iodobenzoic acid (55) under reflux with excess thionyl chloride for several hours[13], and then removing the excess thionyl chloride to give an oily substance which crystallized on standing.



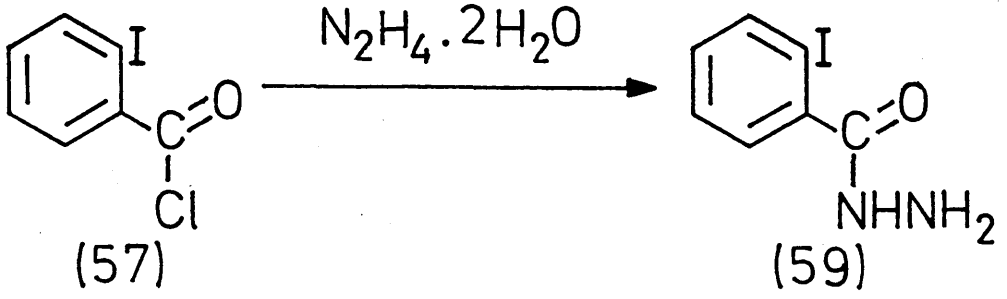
(55) (57)

To these crystals, an excess of concentrated aqueous ammonia was added, dropwise, with stirring. On completion of the exothermic reaction, the brown-coloured benzamide (58) was obtained[14].



(57) (58)

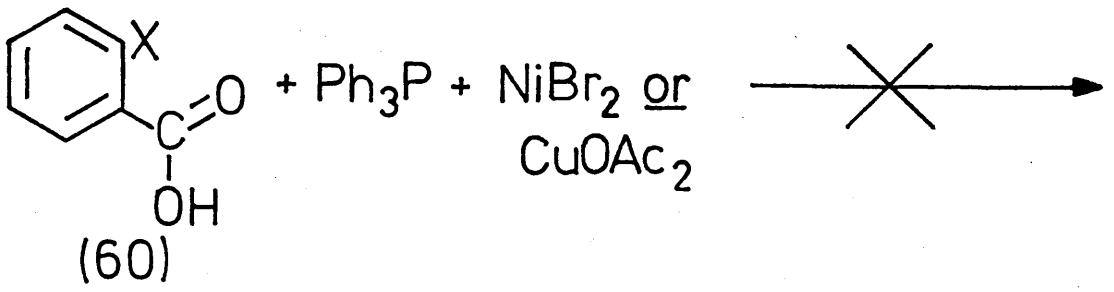
The synthesis of the o-iodobenzhydrazide (59) was achieved using exactly the same conditions as in the preparation of the benzamide (58), but using an excess of hydrazine hydrate instead of ammonia solution.



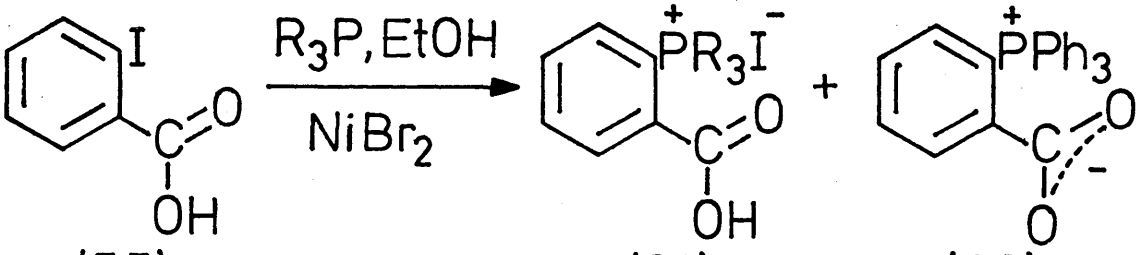
(57) (59)

2.3.2 (B) Reactions

The reactions of the o-halobenzoic acids (60; X = Cl or Br) with triphenylphosphine in the presence of either nickel (II) bromide copper (II) acetate in refluxing ethanol failed to give rise to phosphonium salts. However, the related reaction of o-iodobenzoic acid (55) with triphenylphosphine or tributylphosphine in the presence of only nickel (II) bromide, gave the phosphonium salts (61; R = Ph or Bu) and (for R = Ph) the related betaine (62).



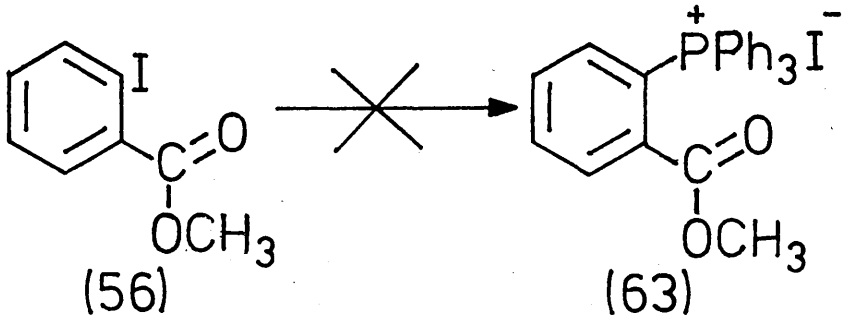
(60)



(55) (61) (62)

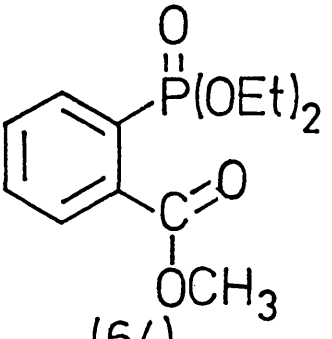
The ^{31}P nmr spectrum of the mixture from the reaction with triphenylphosphine exhibited two signals of equal intensity, at 26.2 (corresponding to the expected phosphonium salt) and 21.7 ppm, respectively, corresponding to the betaine (62). Addition of a strong acid to the solution resulted in the loss of the signal at 21.7 ppm, thus confirming that this signal was due to the presence of the betaine (62). The ^{31}P nmr of the butylphosphonium salt (61; R = Bu) exhibited a signal at 33.2 ppm. Copper (II) acetate failed to catalyse these substitution reactions.

The related o-iodobenzoate ester (56), when treated with triphenylphosphine in the presence of either nickel (II) bromide or copper (II) acetate, did not undergo conversion to the phosphonium salt (63).

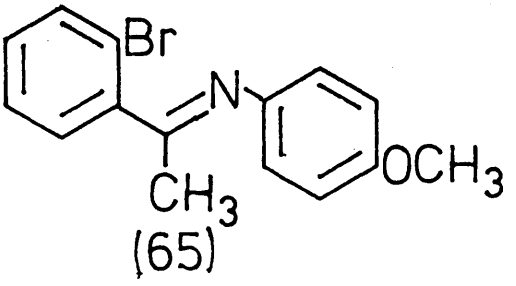


(56) (63)

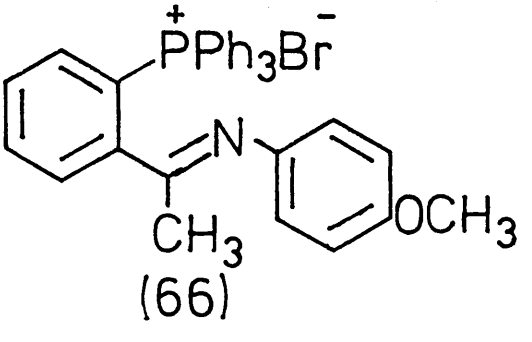
In contrast, Price et al[1], found that the reaction of the ester (56) with triethylphosphite, in the presence of copper (II) acetate, afforded the o-phosphonate ester (64). In comparison, work by Allen et al[10] on the reactions of the stereochemically similar Schiff's base (65) [derived from o-bromoacetophenone with p-anisidine in toluene] has shown that this also undergoes a replacement reaction with triphenylphosphine to give the salt (66).



(64)



(65)



(66)

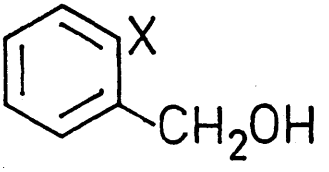
Clearly, three observations can be made:-

(i) the presence of the methyl group on the azomethine carbon causes no steric effect, unlike the methoxy group in the ester (56).

(ii) that different donor atoms (although both being sp^2-hybridized) operate in each situation, thus affecting the reactivity of both molecules in the substitution reaction, and

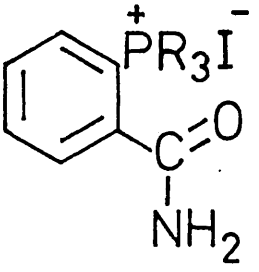
(iii) the course of such a reaction is also dependent on the nature of the tervalent phosphorus compound, and on the metal catalyst.

The o-halobenzyl alcohols (67; X = Br or I) were also found to be inert on prolonged heating in ethanol with tertiary phosphines, in the presence of both nickel (II) and copper (II) ions.

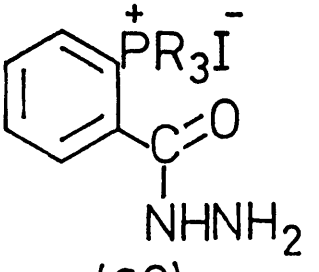


(67)

The reactions of the o-iodobenzamide (58) and the o-iodobenzhydrazide (59) with triphenylphosphine or tributylphosphine in refluxing ethanol containing either nickel (II) or copper (II) ions also failed to yield the corresponding arylphosphonium salts (68; R = Ph or Bu) and (69; R = Ph or Bu).



(68)

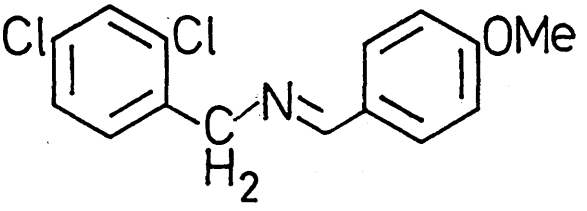


(69)

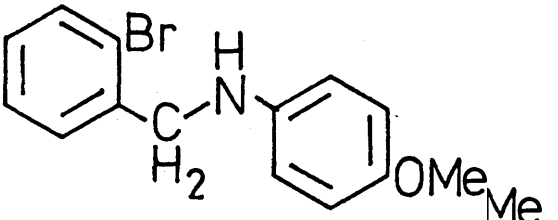
The failure of the above reactions could be attributed to the presence of additional nitrogen (sp^3-hybridised) donor atom(s), which would divert the metal ion away from its role in the catalytic cycle.

2.4 REQUIREMENTS FOR TEMPLATE DESIGN

It is evident that a number of potential template aryl halides which appear to satisfy the effective template criteria of Price[1], nevertheless have proved ineffective in the reactions with tertiary phosphines in the presence of transition-metal ions. Examples of such templates are the Schiff's base (4) and the 'reduced' system (38).

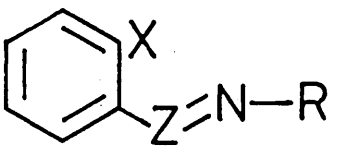


(4)



(38)

In view of these results, a more specific template definition is required. In modifying the template requirements to accommodate the majority of the results presented in this Thesis, it would seem that the most effective system is that in which a halogen atom (except fluorine) is located ortho to a donor group involving an sp^2-hybridised nitrogen atom orientated as in structure (70; Z = CR or N; X = Cl, Br or I; R = non-sterically crowded alkyl or aryl group). The o-haloaryl-Schiff's bases (Z = CR), o-haloarylazo dyestuffs (Z = N), o-halophenylbenzimidazole (18), o-halophenylquinoxaline (29) and the o-halophenylbipyridyl (39) substrates, all clearly fall into this category.



(70)

It is also necessary to recognise the role of the group bound to the sp^2-hybridised nitrogen atom. For the Schiff's base substrates (70; Z = CR), this is clearly of importance, since it has been shown that the presence of bulky groups at the nitrogen, or the presence of an additional donor within that group, which can divert the metal from its catalytic role, have adverse effects on the substitution reaction. In the case of the azo dyestuffs and the o-halophenylbipyridyl substrate (39), the presence of additional donors does not seem to matter.

There is also a crucial interelation between the template and the specific metal ion which is required. In general, for donors with only one donor atom, only nickel (II) is effective as the catalyst [as for the Schiff's bases, the benzimidazole (18) and the quinoxaline (29)], whereas, for the two donor systems, e.g. the o-halophenylbipyridyl system (39), and many of the azo dyestuffs, the reactions are catalysed by both copper and nickel. This aspect will be addressed further in Chapter 3.

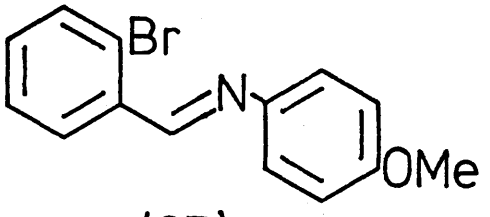
Only two other types of effective template are left, the oxygen donor system (55) and the 1,8-haloiminonaphalene (33), both of which do not conform to the general design

(70). It is interesting that the reactions of these single donor templates are catalysed solely by nickel (II) ions. It is clear that the oxygen template (55) is at the margin of reactivity, since if the halogen is changed to bromine or chlorine, or if the acid function is methylated or converted to the amide/hydrazide derivative, then the template reactivity disappears. The "unexpected" reactivity of the haloiminonaphthalene (33) can doubtless be attributed to the 1,8- (or peri-) position of the substituents on the naphthalene ring. In view of the geometry of the naphthalene system, substituents located at these positions are in much closer proximity than similar substituents located ortho to each other on a benzene ring. This closer proximity has been responsible for the appearance of several unique properties of peri-substituted naphthalenes. Such "proximity effects" have been observed in peri-cyclization reactions[15] as well as in the peri-effects on 1,2-cyclizations[16] and qualitative investigations into the chemical reactivity of peri-substituted naphthalene derivatives[17-19]. Many workers have reported such "proximity effects" in naphthalene chemistry, and this particular subject has attracted increasing attention in recent years.

2.5 REACTIONS AND USES OF TEMPLATE-DERIVED PHOSPHONIUM SALTS

2.5.1 Reactions of Such Phosphonium Salts

Two important reactions have been carried out on the phosphonium salt (71), derived from the Schiff's base (37): (i) reduction using sodium borohydride and (ii) trans-amination.



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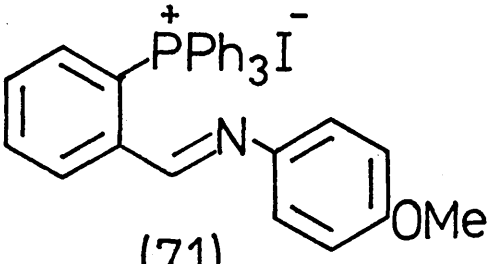

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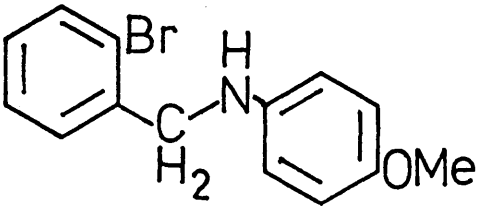
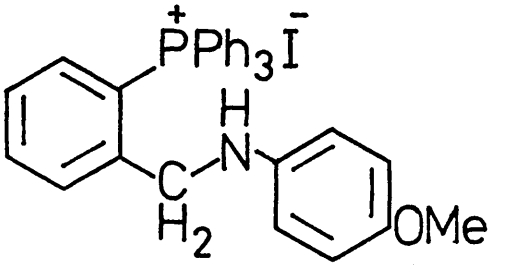


(38)

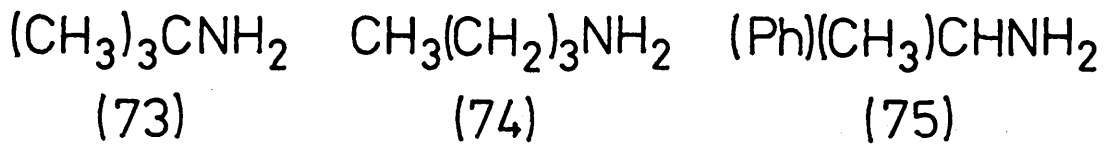


(72)

On treatment with an excess of sodium borohydride in ethanol, the phosphonium salt (71) gave rise to several products as indicated by t.l.c.(Kiessegel 60:40, petrol: chloroform). Repetition of the reaction using equimolar amounts of the salt (71) and sodium borohydride resulted in two developments on tlc, one possibly being the 'reduced' phosphonium salt (72), the other being triphenylphosphine. It is of interest that the salt (72) can not be synthesised from the 'reduced' Schiff's base (38) by direct reaction

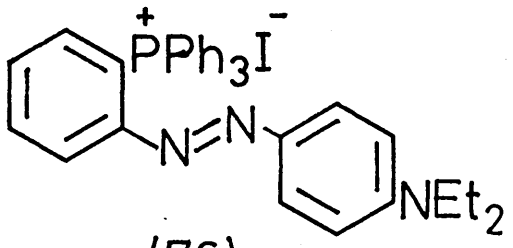
with tertiary phosphine in the presence of nickel (II) ions.

Several attempts at a transamination reaction have been made, but none were successful. The types of amines that were employed were (i) t-butylamine (73), (ii) n-butylamine (74) and (iii) phenylethylamine (75). It is possible that the failure of these reactions can be attributed to the effects of steric crowding at the imino site.

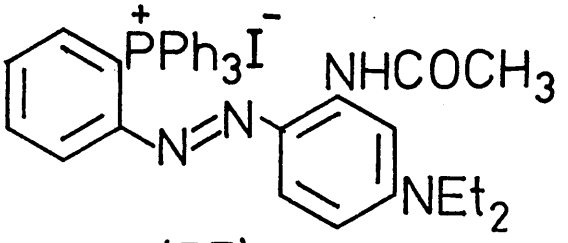


(73) (74) (75)

2.5.2 Uses of Such Phosphonium Salts



(76)



(77)

The two phosphonium salts (76 and 77) have been investigated by Yorkshire Chemicals PLC, Leeds for their potential as cationic dyes. The results show that although they do have some affinity for acrylic fibres, the exhaustion (pick-up of the dye from the liquor to the fabric) achieved was poor. The problem of exhaustion is probably the result of poor dye solubility. Consequently, light and wash fastness tests have been delayed on the dyeings until a satisfactory exhaustion rate can be achieved.

2.6 FAST ATOM BOMBARDMENT (FAB) HIGH RESOLUTION MASS SPECTROMETRY

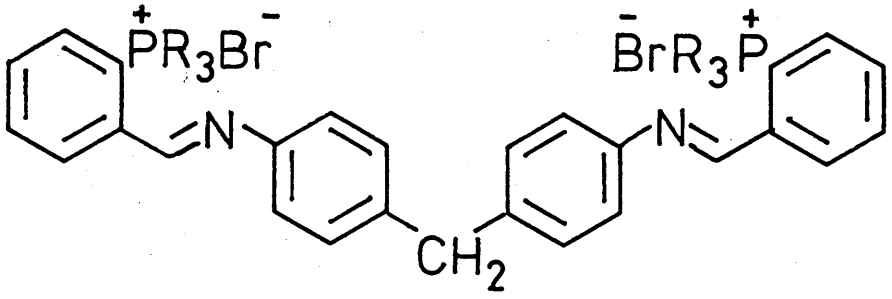
A preliminary investigation into the use of FAB mass spectrometry for the characterisation of phosphonium salts by accurate mass measurement has produced encouraging results. At present, two solvents have been used, the most popular solvent being glycerol[20], and the other being poly(ethyleneglycol) (PEG)[21]. A mixture of different PEG's seems to be the better solvent of the two since it also acts as the calibrant.

A major problem has been encountered when trying to record high resolution FAB spectra of phosphonium salts (including diphosphonium salts). This is the fact that the product is already ionized, and is therefore giving equally strong $[M-Br]^+$ and fragmentation signals, thus making if difficult to observe ions arising from the calibrant.

One solution to this problem, especially in the case of FAB studies, is to use a low resolution spectrum in conjunction with the AMCOR programme[22]. The AMCOR programme only succeeds if it is given two or more theoretical exact mass measurements which are known to arise in the scan of interest (e.g. signals from the reference material). From this, the low resolution masses from the unknown sample which occur in the same scan, are then recorded with a high degree of accuracy. This is permissible because the KRATOS instruments D555/D590 produce masses to an accuracy of four decimal places, even at low resolution.

A low resolution spectrum of the diphosphonium salt (14; R = Bu) using glycerol as the matrix, and the AMCOR programme gave the following result:-

Calculated	$[M-Br]^+$ (^{79}Br)	855.4510
Found	$[M-Br]^+$ (^{79}Br)	855.4489



(14)

The AMCOR result was shown to have a deviation of 2.23 mmu (millimass units). This result is acceptable within the limits (10mmu). However, the spectra of other salts could not be obtained due to the fact that all samples contained insufficient glycerol, i.e. the sample spectra were too strong!

The second, and more profitable solution for FAB characterization was provided by using a glycerol matrix, but employing a mixture of caesium and rubidium iodides as the calibrant. This current modification allows the use of a high resolution run and one example using this approach was the spectrum of the butyl salt (61) derived from o-iodobenzoic acid. This result was shown to have a deviation of 0.54 mmu.

Calculated	$[M-I]^+$	323.2140
Found	$[M-I]^+$	323.2134

2.7 EXPERIMENTAL

Compounds are colourless unless otherwise described. Operations involving aromatic aldehydes and triphenylphosphine were conducted under a nitrogen atmosphere.

Melting points were determined on an Electrothermal melting point apparatus and are uncorrected.

^{1}H Nuclear magnetic resonance spectra were recorded on Brüker WP80 SY and Jeol PMX 60 SI spectrometers at 80 and 60 MHz respectively. Chemical shifts are reported on the δ scale with respect to tetramethylsilane (5% w/v) as an internal standard in deuteriochloroform. Abbreviations used:- s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet.

^{31}P Nuclear magnetic resonance spectra were recorded on a Brüker WP80 SY instrument at 32.4 MHz. Chemical shifts are reported with respect to 85% orthophosphoric acid as an external standard; shifts to high frequency are positive in sign.

High resolution mass spectra, using Fast Atom Bombardment were performed on a Kratos MS80 RFA instrument in a glycerol matrix using a mixture of caesium and rubidium iodides as the reference material. Low resolution mass spectra were recorded on a VG Micromass 30F spectrometer, the matrix used was glycerol.

Microanalyses were determined at the Department of Chemistry, City University, Northampton Square, London, EC1V OHB.

2.7.1 Preparation of Potential Templates

The following compounds have been prepared as previously described:- 8-Bromo-1-naphthylamine (32)[7]; 2-Bromo-N,N-dimethylamine (36)[23]; N-(2-Bromobenzylidene)-4-methoxyaniline (37)[8]; N-(2-Bromobenzyl)-4-methoxyaniline (38)[24]; Bis(tertiary phosphine) nickel (II) chloride (36; R = Ph or Bu)[9]; Tetrakis [bromotriphenylphosphine copper (I)] (48)[11]; 2-Iodomethyl-benzoate (47)[25] and 2-Iodobenzamide (58)[26]; 2-Iodobenzoic acid (55); 2-Halobenzoic acids (60; X = Cl or Br) and 2-Halobenzylalcohols (67; X = Br or I) were obtained commercially and 3-(2,4-Dibromo-5-methylphenyl)-2,2´-dipyridine (39) was supplied by ICI Organics Division, Blakely. The following compounds appear to be new.

The Synthesis of the Bis-Schiff's Bases

These were prepared by heating together 2-Bromobenz-aldehyde (2 moles) with the appropriate α-ω diamine (1 mole) in refluxing ethanol for 60-90 minutes. Compounds (9), (10) and (11) were prepared using the same conditions with replacement of the α-ω diamine by 4,4´-methylenedianiline, p-phenylenediamine and 2,2´-diaminobiphenyl, respectively. The latter diamine was prepared from 2,2´-dinitrobiphenyl as described by R.W. West[27]. In all cases, the bis-Schiff's bases crystallized on cooling and were purified by re-crystallisation.

N,N´-Bis-(2-bromobenzylidene)azine (8; n = 0). This was isolated as yellow crystals, (98%), m.p. 177°C (from $CHCl_3$/EtOH). (Found: C 45.71; H 2.64; N 7.53: $C_{14}H_{10}N_2Br_2$

requires C 45.93; H 2.75; N 7.65%) δ^1H($CDCl_3$) 8.6(s,2H) 8.1-7.1(m,8ArH)ppm.

N,N´-Bis-(2-bromobenzylidene)ethane-1,2-diamine (8; n = 2) (90%). This had m.p. 97°C (from EtOH). (Found; C 48.85; H 3.75; N 7.09: $C_{16}H_{14}N_2Br_2$ requires C 48.75; H 3.60; N 7.11%), δ^1H($CDCl_3$) 8.6(s,2H), 8.1-7.2(m,8ArH) 4.0(s,4H) ppm.

N,N´-Bis-(2-bromobenzylidene)propane 1,3-diamine (8; n = 3) (88%), m.p. 65°C (from EtOH), (Found: C 50.01; H 3.90; N 6.87: $C_{17}H_{16}N_2Br_2$ requires C 50.02; H 3.95; N 6.86%), δ^1H ($CDCl_3$) 8.6(s,2H) 8.1-7.2(m,8ArH) 3.8(t,4H) 2.1(qn,2H) ppm.

N,N´-Bis-(2-bromobenzylidene)butane 1,4-diamine (8; n = 4) (81%) m.p. 51°C (From EtOH), (Found C 51.23; H 4.29; N 6.52: $C_{18}H_{18}N_2Br_2$ requires C 51.21; H 4.29; N 6.63%), δ^1H ($CDCl_3$) 8.6(s,2H) 8.1-7.2(m,8ArH) 3.7(s,4H) 1.8(s,4H) ppm.

N,N´-Bis-(2-bromobenzylidene)pentane 1,5-diamine (8; n = 5) This was obtained as a pale cream solid (74%) m.p. 48°C (from EtOH), (Found C 52.30; H 4.60; N 6.31: $C_{19}H_{20}N_2Br_2$ requires C 52.31; H 4.62; N 6.42%), δ^1H ($CDCl_3$) 8.6(s,2H) 8.1-7.2(m,8ArH) 3.7(t,4H) 1.8(q,6H) ppm.

N,N´-Bis-(2-bromobenzylidene)hexane-1,6-diamine (8; n = 6) (85%) m.p. 73°C (from EtOH), (Found C 53.44; H 4.90; N 6.09: $C_{20}H_{22}N_2Br_2$ requires C 53.35; H 4.92; N 6.22%) δ^1H($CDCl_3$) 8.6(s,2H) 8.1-7.1(m,8ArH) 3.6(t,4H) 1.6(m,8H) ppm.

N,N´-Bis-(2-bromobenzylidene)heptane-1,7-diamine (8; n = 7) (73%) m.p. 48°C (from EtOH), (Found C 54.51; H 5.18; N 6.03:

$C_{21}H_{24}N_2Br_2$ requires C 54.33; H 5.21; N 6.03%) $\delta^1H(CDCl_3)$ 8.6(s,2H) 8.1-7.2(m,8ArH) 3.6(t,4H) 1.6(m,10H)ppm.

N,N´-Bis-(2-bromobenzylidene)octane-1,8-diamine (8; n = 8) (81%) m.p. 52°C (from EtOH), (Found C 55.31; H 5.50; N 5.87: $C_{22}H_{26}N_2Br_2$ requires C 55.24; H 5.47; N 5.85%), $\delta^1H(CDCl_3)$ 8.6(s,2H) 8.1-7.2(m,8ArH) 3.7(t,4H) 1.1(m,12H)ppm.

N,N´-Bis-(2-bromobenzylidene)dodecane-1,12-diamine (8; n = 12) This was obtained as pale yellow crystals (65%) m.p. 53°C, (from EtOH), (Found C 58.50; H 6.40; N 5.24: $C_{26}H_{34}N_2Br_2$ requires C 58.44; H 6.41; N 5.24%) $\delta^1H(CDCl_3)$ 8.6(s,2H) 8.1-7.1(m,8ArH) 3.7(t,4H) 1.5(m,20H)ppm.

N,N´-Bis-(2-bromobenzylidene)4,4´-diaminodiphenylmethane (9) This was isolated as pale yellow crystals (83%) m.p. 142°C (from EtOH), Found C 60.74; H 3.73; N 5.25: $C_{27}H_{20}N_2Br_2$ requires C 60.92; H 3.78; N 5.26%) $\delta^1H(CDCl_3)$ 8.8(s,2H) 8.3-7.2(m,16ArH) 4.0(s,2H) ppm.

N,N´-Bis-(2-bromobenzylidene)1,4-diaminobenzene (10) This was obtained as bright yellow coloured crystals (92%) m.p. 157°C (From petrol 60/40), (Found C 54.32; H 3.10; N 6.15: $C_{20}H_{14}N_2Br_2$ requires C 54.32; H 3.19; N 6.33%) δ^1H $(CDCl_3)$ 8.9(s,2H) 8.4-7.3(m,12ArH)ppm.

N,N´-Bis-(2-bromobenzylidene)biphenyl-2,2´-diamine (11) This was isolated as yellow crystals (68%) m.p. 108°C (from EtOH), (Found C 60.25; H 3.45; N 5.30: $C_{26}H_{18}N_2Br_2$ requires C 60.25; H 3.45; N 5.40%), $\delta^1H(CDCl_3)$ 8.5(s,2H) 8.0-6.5(m,16ArH)ppm.

The Synthesis of Other Potential Templates

1-(2-Bromobenzyl)2-(2-bromophenyl)benzimidazole (18)

To a solution of o-phenylene diamine (1.1g, 0.01 moles) in ethanol (20 cm^3) was added 2-bromobenzaldehyde (3.7g, 0.02 moles), and the resulting mixture heated under reflux for 2-3 hours. On cooling, a pale yellow crystalline solid was formed. This was recrystallised from ethanol to give the 1-(2-Bromobenzyl)2-(2-Bromophenyl)benzimidazole (1.1g, 25%), m.p. 117.5°C (Found C 54.05; H 3.10: N 6.25: $C_{20}H_{14}N_2Br_2$ requires C 54.30: H 3.20; N 6.35%) $\delta^1H(CDCl_3)$ 8.0-6.5(m,12ArH), 5.3(s,2H) ppm. [m/e 442 (M^+) (100%); 361 ($M-^{81}Br$) (45%) and 169 (65%)].

2,3-Bis-(2-chlorophenyl)quinoxaline (29)

To a stirred solution of o-phenylene diamine (2.2g, 0.02 moles) in ethanol (50cm^3), was added 2,2´-dichlorodibenzoyl (5.58g, 0.02 moles). The solution was heated under reflux under nitrogen for 2 hours. On cooling pale cream crystals formed. This was recrystallised from ethanol to give the 2,3-Bis-(2-chlorophenyl)quinoxaline (6.9g, 98%) m.p. 116-118°C (from EtOH), (Found C 68.50; H 3.45; N 7.96: $C_{20}H_{12}N_2Cl_2$ requires C 68.39; H 3.44; N 7.97%).

1-(N-Benzylidene)imino-8-bromonaphthalene (33)

A mixture of 8-bromo-1-naphthylamine[7] (1.0g, 4.5×10^{-3} moles) and benzaldehyde (0.48g, 4.5×10^{-3}moles) in ethanol (10cm^3) with a catalytic amount of p-toluene sulphonic acid was refluxed under nitrogen for 2 hours. After filtration the solid was recrystallised giving (0.9g, 59%) m.p. 97°C

(from MeOH), (Found C 66.14, H 4.03, N 4.43, $C_{17}H_{12}N_1Br_1$ requires C 65.82, H 3.89, N 4.51%) δ^1H ($CDCl_3$) 8.4(s,1H) 8.1-6.8(m,11ArH) ppm.

2-Iodobenzhydrazide (59) (prepared by a modification of the general procedure in Vogel[13,14]). To a flask containing redistilled thionyl chloride (32.6g, 20cm^3, 0.28 moles), 2-Iodobenzoic acid (10g, 0.04 moles) was added slowly, and the mixture was heated on a water bath for 30 minutes. On addition of all the acid the mixture was heated for a further 30 minutes. Isolation of the crude acid chloride was achieved by distilling off the excess thionyl chloride. On standing overnight red crystals of 2-Iodobenzylchloride formed. The crystals were filtered and washed with petrol (9.17g, 86%). The crude acid chloride (5.0g, 0.02 moles) was added, dropwise, with excessive stirring to a freezing solution of hydrazine hydrate (25cm^3, 64% w/v). Following the exothermic reaction the hydrazide crystallized out on standing. After filtration the product was recrystallized giving 2-Iodobenzhydrazide (3.1g, 63%) m.p. 192°C, (Found C 33.05, H 2.58, N 10.09: $C_7H_7O_1N_2I_1$ requires C 32.06; H 2.67; N 10.68%) δ^1H ($(CD_3)_2CO$) 10.0(s,1H) 7.9(d,1ArH) 7.4(m,3ArH) 2.1(s,2H) ppm.

2.7.2 Preparation of Bis Phosphonium Salts

General Procedure for the Reactions of Bis Schiff's Base with Phosphines

The bis-Schiff's base (10^{-3}mol), tertiary phosphine (5×10^{-3}mole) and nickel (II) bromide (2×10^{-4}mol equiv.) were heated together under reflux in ethanol (10cm^3) in

a nitrogen atmosphere for 5-8 hours, and the progress of the reaction was monitored by t.l.c. [Kieselgel; $CHCl_3$-EtOH (90:10) as the elutant]. The reaction mixture was then poured into water (50cm^3) containing KBr (0.5g), and extracted with ether (2 x 20cm^3) in order to remove non-ionic impurities. The aqueous layer was then extracted with chloroform (3 x 10cm^3) and discarded. The chloroform layer was dried ($MgSO_4$) and evaporated. The oily residue was then triturated several times with sodium-dried ether until it solidified. On filtration, the majority of bis-phosphonium salts, when in contact with the atmosphere, changed almost instantaneously from light-brown solids into dark-brown sticky amorphous compounds. Several of the bis-phosphonium salts that were not hygroscopic were recrystallised from chloroform-ethyl acetate (except as stated otherwise). Characterization by microanalysis proved to be impossible on the hygroscopic salts even on conversion to their related mecuric bromide, tetra-fluroborate, perchlorate or picrate salts. High resolution fast-atom bombardment (FAB) mass spectrometry has been employed with some success, although in the aliphatic bridged diphosphonium salts no molecular ion or $(M-Br)^+$ signal has been observed. The following salts have been characterised:-

<u>N,N´-Bis-(2-triphenylphosphoniobenzylidene)azine dibromide</u> (13; n = 0). This was isolated as bright yellow crystals, (70%) m.p.>300°C (from $CHCl_3$/ether), (Found C 63.30; H 4.59; N 2.96; $C_{50}H_{40}N_2Br_2P_2.3H_2O$ requires C 63.56; H 4.87; N 2.97%) $\delta^{31}P$ ($CDCl_3$): 26.34 ppm; δ^1H ($CDCl_3$) 8.6(s,2H) 8.2-7.1(m,38ArH) ppm.

N,N´-Bis-(2-triphenylphosphoniobenzylidene)propane 1,3 diamine dibromide (13; n = 3). This was obtained as a hygroscopic brown solid (∿25%) $\delta^{31}P(CDCl_3)$ 24.60 ppm; $\delta^{1}H(CDCl_3)$ 8.65(s,2H) 8.2-7.2(m,38ArH) 2.2(t,4H) 0.4(qn,2H) ppm.

N,N´-Bis-(2-triphenylphosphoniobenzylidene)butane-1,4-diamine dibromide (13; n = 4). A brown hygroscopic solid isolated in 65% yield $\delta^{31}P(CDCl_3)$ 24.23ppm; $\delta^{1}H(CDCl_3)$ 8.7(s,2H) 8.1-7.0(m,38ArH) 2.2(s,4H) 0.8(s,4H)ppm.

N,N´-Bis-(2-triphenylphosphoniobenzylidene)pentane-1,5-diamine dibromide (13; n = 5). This was isolated as a hygroscopic brown solid (∿60%) $\delta^{31}P(CDCl_3)$ 24.68ppm; $\delta^{1}H(CDCl_3)$ 8.6(s,2H) 8.2-7.2(m,38ArH) 2.5(t,4H) 0.5 (q,6H)ppm.

N,N´-Bis-(2-triphenylphosphoniobenzylidene)hexane-1,6-diamine dibromide (13; n = 6). This was obtained as a hygroscopic brown solid (∿68%) $\delta^{31}P(CDCl_3)$ 24.69ppm; $\delta^{1}H(CDCl_3)$ 8.8(s,2H) 8.5-7.4(m,38ArH) 2.2(t,4H) 0.8(m,8H)ppm.

N,N´-Bis-(2-triphenylphosphoniobenzylidene)heptane 1,7-diamine dibromide (13; n = 7). Isolated as a hygroscopic brown solid (∿70%) $\delta^{31}P(CDCl_3)$ 24.78ppm; $\delta^{1}H(CDCl_3)$ 8.5(s,2H) 8.2-7.1(m,38ArH) 2.6(t,4H) 0.7(m,10H)ppm.

N,N´-Bis-(2-triphenylphosphoniobenzylidene)octane 1,8-thiamine dibromide (13; n = 8). Brown hygroscopic solid (∿62%) $\delta^{31}P(CDCl_3)$ 24.69ppm; $\delta^{1}H(CDCl_3)$ 8.6(s,2H) 8.1-7.2(m,38ArH) 2.7(t,4H) 0.7(m,12H)ppm.

N,N´-Bis-(2-triphenylphosphoniobenzylidene)dodecane 1,12-diamine dibromide (13; n = 12). This was isolated as a hygroscopic brown solid (∿ 63%) $\delta^{31}P(CDCl_3)$ 25.05 ppm; $\delta^{1}H(CDCl_3)$ 8.35(s,2H) 8.1-7.3(m,38ArH) 2.7(t,4H) 0.8(m,20H) ppm.

N,N´-Bis-(2-triphenylphosphoniobenzylidene)4,4´-diamino-phenylmethane dibromide (14; R = Ph). This was isolated as yellow crystals (70%) m.p.>300°C (from EtOH/EtOAc). (Found C 67.09; H 4.65; N 2.47: $C_{63}H_{50}N_2Br_2P_2 . 4H_2O$ requires C 67.02; H 5.14; N 2.48%) $\delta^{31}P(CDCl_3)$ 25.89 ppm; $\delta^{1}H$ ($CDCl_3$) 8.65(s,2H) 8.2-7.2(m,38ArH) 6.75-5.95(8ArH, deceptively simple $[AX]_2$ system) 3.65(s,2H)ppm. [Found $(M-^{81}Br)^+$ 975.2647 $C_{63}H_{50}N_2P_2Br_2$ requires $(M-^{81}Br)^+$ 975.2632].

N,N'-Bis-(2-tributylphosphoniobenzylidene)4,4´-diamino-phenylmethane dibromide (14; R = Bu). This was isolated as yellow crystals (67%) m.p. >300°C (from $CHCl_3$/EtOAc). (Found C 63.79; H 7.92; N 2.88; $C_{51}H_{74}N_2Br_2P_2$ requires C 64.15; H 7.97; 2.94%). $\delta^{31}P(CDCl_3)$ 34.01 ppm; $\delta^{1}H$ ($CDCl_3$) 8.8(s,2H) 8.0(m,8ArH) 7.3(s,8ArH) 4.1(s,2H) 2.95(m,12H) 1.50(m,24H) 0.8(m,18H) ppm. [Found $(M-^{81}Br)^+$ 855.4489 $C_{51}H_{74}N_2Br_2P_2$ requires $(M-^{81}Br)^+$ 855.4510].

N,N´-Bis-(2-triphenylphosphoniobenzylidene)1,4-diamino-benzene dibromide (15; R = Ph). This was isolated as orange crystals (76%) m.p.>300°C (from $CHCl_3$/EtOAc). (Found C 67.62; H 4.59; N 2.78: $C_{56}H_{44}N_2Br_2P_2 . 2H_2O$ requires C 67.07; H 4.79; N 2.79%) $\delta^{31}P(CDCl_3)$ 25.86 ppm; $\delta^{1}H(CDCl_3)$ 8.75(s,2H) 7.9-7.3(m,42ArH) ppm.

N,N'-Bis-(2-tributylphosphoniobenzylidene)1,4-diamino-benzene dibromide (15; R = Bu). This was isolated as a hygroscopic orange solid. $\delta^{31}P(CDCl_3)$ 33.60 ppm $\delta^{1}H(CDCl_3)$ 8.7(s,2H) 8.1-7.3(m,12ArH) 2.80(m,12H) 1.40(m,24H) 0.9(m,18H) ppm.

General Preparation of Quinoxaline Diphosphonium Salts

The quinoxaline (10^{-3}mole), bis(tertiary phosphine) nickel (II) chloride (10^{-3}mole) and an extra mole of the appropriate tertiary phosphine were heated together under reflux in ethanol in a nitrogen atmosphere for 6-8 hours. The same work-up as described earlier (section 2.7.2) was employed and the following salts were isolated.

2,3-Bis-(2-triphenylphosphoniophenyl)quinoxaline dibromide (43; R = Ph). A cream solid (50%) m.p. 270°C decomp. (from $CHCl_3$/EtOAc). (Found C 69.09; H 4.87: $C_{56}H_{42}N_2Cl_2P_2$. $CHCl_3$ requires C 68.79; H 4.32%). $\delta^{31}P(CDCl_3)$ 26.73 ppm.

2,3-Bis-(2-tributylphosphoniophenyl)quinoxaline dibromide (43; R = Bu). A cream solid was collected (41%) m.p. 240°C decomp. (from $CHCl_3$/ether). (Found C 64.30; H 8.42; N 3.35: $C_{44}H_{66}N_2Cl_2P_2 \cdot 4H_2O$ requires C 63.84; H 8.95; N 3.39%) $\delta^{31}P(CDCl_3)$ 32.96 ppm; $\delta^{1}H(CDCl_3)$ 8.1(m,4ArH) 7.6(m,8ArH) 2.85(m,12H) 1.45(m,24H) 0.8(m,18H) ppm.

2.7.3 Preparation of Mono Phosphonium Salts

General Procedure. The template (10^{-3}mole), tertiary phosphine (3×10^{-3}moles) and nickel (II) bromide (2×10^{-3} moles) were heated together under reflux in ethanol ($10cm^3$)

in a nitrogen atmosphere for 5-8 hours. The general isolation procedure described in section 2.7.2 was employed to obtain the monophosphonium salts. Copper (II) acetate (2×10^{-3}moles) can be used in place of nickel (II) bromide to promote the substitution reaction when oxygen donor molecules and certain types of double donor molecules (cf Price's type III halide) are employed. The following salts have been characterised:-

Triphenyl-2-(1-(2-bromobenzyl)-2-benzimidazoyl)phenyl phosphonium bromide (41; R = Ph). This was isolated as yellow crystals (54%) m.p. 285°C (from $CHCl_3$-EtOAc). (Found C 59.25; H 3.95; N 3.50: $C_{38}H_{29}N_2Br_2P_2$ $0.5CHCl_3$ requires C 60.50; H 3.85; N 3.65%) $\delta^{31}P(CDCl_3)$ 25.14 ppm; $\delta^{1}H(CDCl_3)$ 8.0-6.5(m,27ArH) 5.0(s,2H).

Tributyl-2-(1-(2-bromobenzyl)-2-benzimidazoyl)phenyl phosphonium bromide (41; R = Bu). This was obtained as a yellow solid (46%) m.p. 130-134°C decomp. (from $CHCl_3$ -EtOAc). (Found C 49.80; H 5.79; N 3.92: $C_{32}H_{41}N_2Br_2P_1B_1F_4$ requires C 49.85; H 5.29; N 3.49%) $\delta^{31}P(CDCl_3)$ 32.78 ppm; $\delta^{1}H(CDCl_3)$: 8.3-6.6(m,12ArH) 5.3(s,2H) 2.45(m,6H) 1.4(m,12H) 0.8(m,9H)ppm.

8-(N-Benzylidene)amino-1-naphthyltriphenylphosphonium bromide (45). This was isolated as a pale yellow solid (67%) m.p. 90-95°C decomp. (from $CHCl_3$/EtOAc). (Found C 72.25; H 4.72; N 2.36: $C_{35}H_{27}N_1P_1Br_1$ $0.5H_2O$ requires C 72.29; H 4.82; N 2.41%) $^{31}P(CDCl_3)$ 24.18 ppm. $^{1}H(CDCl_3)$ 8.5(d,1H) 8.3-6.3(m,26ArH)ppm.

3-(2-Triphenylphosphonio-4-bromo-5-methylphenyl)2,2´-bipyridyl bromide (47; R = Ph) (40%) m.p.272°C (from $CHCl_3$/EtOAc). (Found C 60.52; H 4.24; N 4.03: $C_{35}H_{27}N_2Br_2P_1$. $2H_2O$ requires C 59.83; H 4.13; N 3.99%) $\delta^{31}P(CDCl_3)$ 23.89 ppm; $\delta^{1}H(CDCl_3)$ 8.2-7.0(m,24ArH) 2.7(s,3H) ppm. [Found $(M-^{81}Br)^+$ 585.1079 $C_{35}H_{27}N_2Br_2P_1$ requires $(M-^{81}Br)^+$ 585.1095]

3-(2-Tributylphosphonio-4-bromo-5-methylphenyl)2,2´-bipyridyl bromide (47; R = Bu) (42%) m.p. 134°C (from $CHCl_3$/ether). (Found C 56.43; H 6.37; N 4.57: $C_{29}H_{39}N_2Br_2P_1$. H_2O requires C 55.77; H 6.57; N 4.49%) $\delta^{31}P(CDCl_3)$ 32.79 ppm; $\delta^{1}H(CDCl_3)$ 8.8-7.4(m,9ArH) 2.6(m,9H) 1.4(m,12H) 0.9(m,9H) ppm.

2-Carboxyphenyltriphenylphosphonium iodide (61; R = Ph). This was isolated as a cream coloured solid (44%) m.p. 120°C (from $CHCl_3$/ EtOAc). (Found C 57.23; H 4.67: $C_{25}H_{20}I_1O_2P_1$. H_2O requires C 56.82; H 4.17%) $\delta^{31}P(CDCl_3)$ 26.18 ppm; $\delta^{1}H(CDCl_3)$ 9.8(s,1H) 7.8(m,19ArH) ppm.

2-Carboxyphenyltributylphosphonium iodide (61; R = Bu). This was obtained as a light brown solid (56%) m.p. 184°C (from $CHCl_3$/ether). (Found C51.18; H 7.46: $C_{19}H_{32}I_1O_2P_1$ requires C 50.66; H 7.11%) $\delta^{31}P(CDCl_3)$ 34.98 ppm; $\delta^{1}H(CDCl_3)$ 9.7(s,1H) 8.6-7.7(m,4ArH) 2.7(m,6H) 1.5(m,12H) 0.9(m,9H) ppm. [Found $(M-I)^+$ 323.2134 requires $(M-I)^+$ 323.2140].

4-Methoxy-N-(2-triphenylphosphoniobenzylidene)aniline iodide (71). This was isolated as bright yellow crystals (56%) m.p. 281°C (from $CHCl_3$/EtOAc), (Found C 63.82; H 4.49; N 2.53: $C_{32}H_{27}N_1I_1P_1O_1$ requires C 64.11; H 4.53; N 2.33%) $\delta^{31}P(CDCl_3)$ 25.94 ppm $\delta^{1}H(CDCl_3)$ 8.6(s,1H) 8.5-7.0(m,19ArH)

6.7-5.9(deceptively simple $[AX]_2$ system, 4ArH) 3.7(s,3H) ppm.

4-Methoxy-N-(2-triphenylphosphoniobenzyl)aniline iodide (72). To a solution of the salt (71; 0.5g, $9\text{-}3\text{x}10^{-4}$moles) in ethanol ($10cm^3$) was added an equimolar amount of sodium borohydride (0.04g). The resulting mixture was heated under reflux for 1 hour. The cooled mixture was then poured into water ($75cm^3$) and the product was filtered off. The product was recrystallised from chloroform/ether to yield pale yellow crystals (0.31g, 62%) m.p.>300°C (from $CHCl_3$/ether) $\delta^{31}P(CDCl_3)$ 22.22 ppm. $\delta^{1}H(CDCl_3)$ 8.1-7.4(m,19ArH) 6.6-5.8(simple $[AX]_2$ system, 4ArH) 3.7(s,3H) 2.2(s,1H) 1.7(s,2H) ppm.

Bromo(triphenylphosphine)(3-(2,4-dibromo-5-methylphenyl) -2,2'-bipyridyl) copper (I) (49). On the addition of ethanol ($10cm^3$) and heat to a colourless equimolar mixture of the aryl halide (39; 0.25g, 6.15×10^{-4}moles) and the copper (I) phosphine complex (48; 0.25g) an orange-red coloured solution appeared. On cooling red crystals were isolated and recrystallised from ethanol to give (0.34g, 61.9%) m.p. 202-204°C (from EtOH). (Found C 51.55; H 3.16, N 3.39: $C_{35}H_{27}N_2Br_3P_1Cu_1$ requires C 51.90; H 3.36; N 3.45%) $\delta^{31}P(CDCl_3)$ -4.96 ppm $\delta^{1}H(CDCl_3)$ 8.2-7.1(m,24ArH) 2.4(s,3H) ppm.

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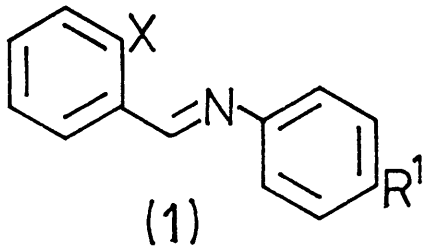
CHAPTER 3: A KINETIC STUDY OF THE NICKEL (II) ION-CATALYSED REACTIONS OF ORTHO-HALOARYL-SCHIFF'S BASE AND - AZO DYESTUFF TEMPLATES WITH TERTIARY PHOSPHINES

3.1 INTRODUCTION

This chapter presents a kinetic study of two examples of the template-assisted substitution reactions discussed earlier: (i) the nickel (II) catalysed reactions of a series of o-haloaryl-Schiff's bases (1; X=Cl, Br or I; R^1=OMe, H, Me, Br, OH, CN, NO_2, $COEt_2$, NHPh or NEt_2) with tertiary phosphines to give the phosphonium salts (2; R^1=OMe, H, Me, Br, OH, $COEt_2$, NHPh or NEt_2; R^2=Ph or Bu); and (ii) the related reactions of the o-haloarylazodyestuffs (3; X=Cl, Br or I; R^1=H or NHCOMe) to give the corresponding phosphonium salts (4; R^1=H or NHCOMe; R^2=Ph or Bu).



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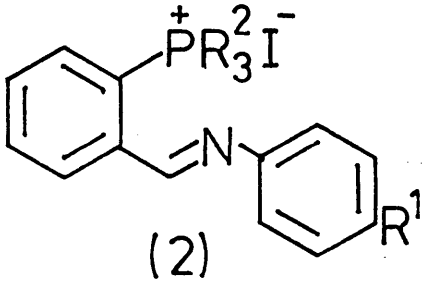

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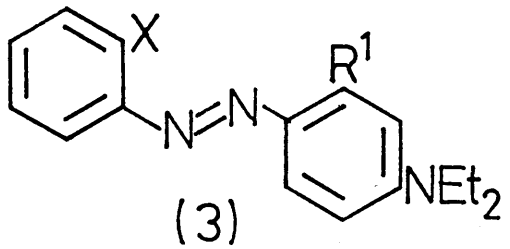

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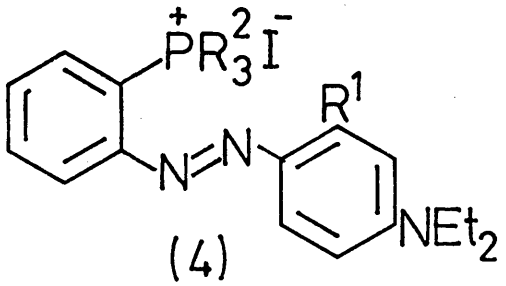

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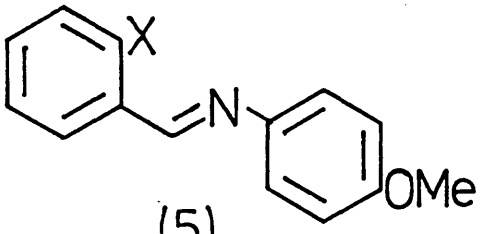
It was envisaged that the progress of these reactions could be followed by observing the formation of the phosphonium salts either (i) by monitoring the increase in conductivity of the system or (ii) by observing the increase in the U.V. - visible absorbance of the solutions

with respect to time. Factors which might affect the rate of the reaction are also discussed, including (a) the nature of the halogen displaced, (b) the nature of the solvent, (c) the identity of the metal ion catalyst, (d) the effect of substituents in the remote aryl ring, (e) the effect of potential inhibitors, e.g. radical scavengers, and (f) the nature of the phosphine.

3.2 PREPARATION OF SCHIFF'S BASE AND AZODYESTUFF TEMPLATES USED IN THE KINETIC STUDY

3.2.1 Synthesis of Ortho-Haloaryl Schiff's Bases

The synthesis of the Schiff's bases (5; X=F, Cl or Br) was achieved by the reaction of the readily available o-halobenzaldehyde with an equimolar amount of p-anisidine in refluxing ethanol under an inert atmosphere for 1-2 hours. The Schiff's base (5; X=I) was prepared using the same conditions except that o-iodobenzaldehyde was prepared by the pyridinium chlorochromate oxidation of o-iodobenzyl alcohol in dichloromethane. The products crystallised on cooling, giving yellow solids in high yields (c.a. 60%).



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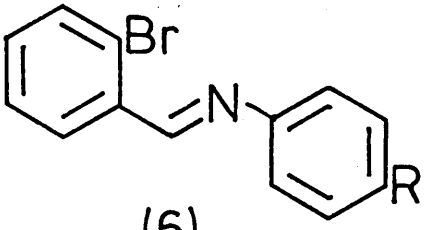


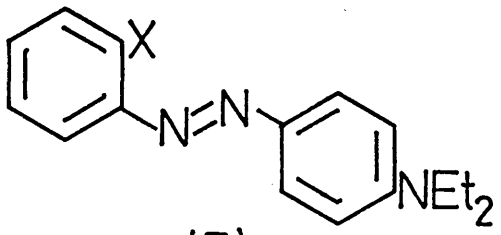
(6)

A similar approach was employed in the synthesis of the Schiff's bases (6; R=H, Me, Br, OH, CN, NO_2, CO_2Et, NHPh or NEt_2) bearing a range of substituents in the para-position of the remote aryl ring. All these templates were isolated as crystalline solids except (6; R=H) which was a viscous liquid.

3.2.2 Synthesis of Ortho-Haloarylazo Dyestuffs

The synthesis of a range of azodyestuffs of types (7; X=Cl, Br or I) and (8; X=Cl, Br or I) was achieved

by the diazotisation of the o-haloaniline followed by a coupling reaction with either N,N-diethylaniline or m-acetylamino-N,N-diethylaniline, respectively, under mildly acidic conditions. The dyes were purified by recrystallisation from ethanol.



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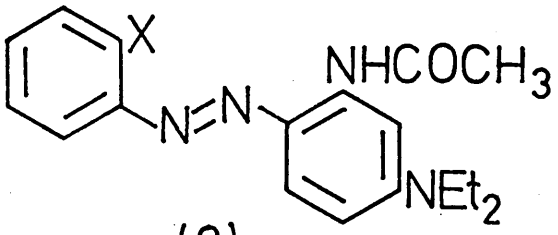

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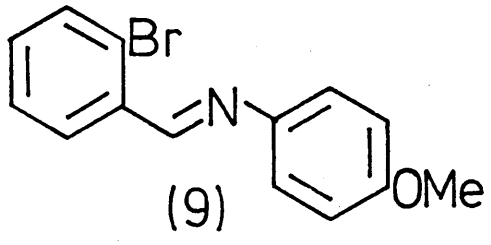
3.3 PRELIMINARY RATE STUDIES

3.3.1 An Investigation of a Range of Potential Metal Salt Catalysts

It has been demonstrated that when the Schiff's base (9) is heated under reflux in ethanol in a nitrogen atmosphere with triphenylphosphine (2 mol equiv.) in the presence of nickel (II) bromide (0.5 mol equiv.) it is converted to the salt (10; R=Ph) in high yield.[1]



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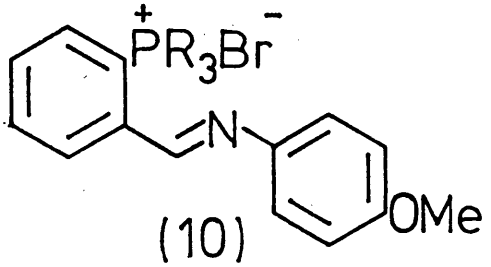


(10)

From earlier work it was found that the reaction did not proceed in the presence of copper (II) acetate (cf the related reaction of the o-bromodiarylazo dyestuffs)[2].

To extend this study, a range of transition metal salts was used in place of nickel (II) bromide. The salts used were:

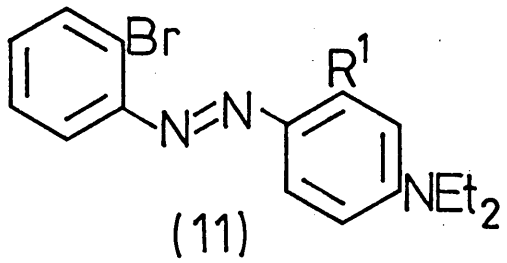
cobalt (II) bromide;	cobalt (II) acetate;
manganese (III) acetate;	manganese (II) chloride;
chromium (III) chloride;	zinc (II) chloride;
iron (III) chloride;	iron (II) chloride.

In addition, two non-transitional metal salts, tin (II) chloride and aluminium (III) chloride, were also investigated.

Thin layer chromatography was used to monitor the progress of the reactions [solvent system 95% $CHCl_3$: 5% EtOH).

For comparison a commercially available phosphonium salt, tetraphenylphosphonium bromide ($Ph_4P^+Br^-$), together with the salt (10; R=Ph), were employed as t.l.c. markers. Detection of the phosphonium salts was achieved easily on immersion of the t.l.c. plates in an iodine vapour bath. A characteristic bullet-shaped development appeared due to a phosphonium salt-iodine adduct being formed. The ^{31}P n.m.r. spectra were also recorded for all of the isolated solids. Only one reaction, that involving cobalt (II) bromide as catalyst, resulted in a ^{31}P n.m.r. signal which corresponded to the expected phosphonium salt (10; R=Ph) signal at 25.8ppm. However, the isolated yield was poor in comparison to that from the nickel (II) catalysed reaction (< 20% after 3 days reflux). Thus, only nickel (II) salts appear to catalyse the replacement reaction to give reasonable yields of phosphonium salts (> 95% after 24 hours). All the other potential catalysts (except cobalt (II) bromide) are either ineffective or give rise to products other than the expected salt (9). In certain cases (e.g. with iron (II) chloride) evidence from ^{31}P n.m.r. studies suggest that the product is more likely to be a transition-metal-phosphine complex.

A similar study on the azodyestuffs (11; R^1=H or NHCOMe) revealed that only nickel (II) and not copper (II) salts catalysed the replacement reaction to give the salts (12; R^1=H or NHCOMe; R^2=Ph or Bu). These findings contrast with the phosphonation reactions reported by Hall and Price [3,4], who showed that such reactions of the dyes



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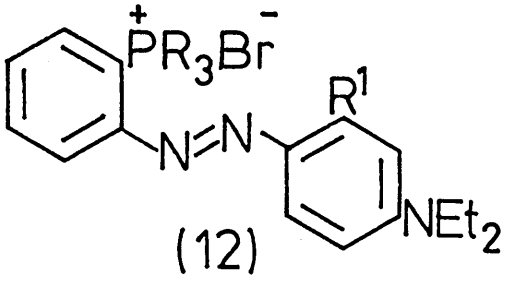
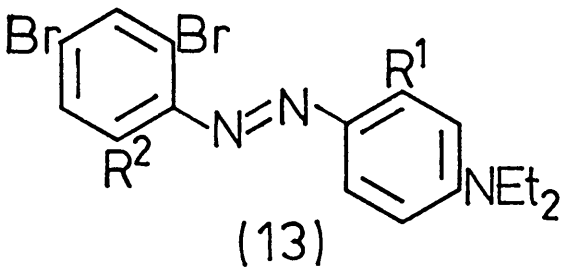


(12)

(13; R^1=H or NHCOMe) catalysed by copper (II) acetate, are sensitive to the steric effects of substituents (R^2) in the aryl ring carrying the bromine atom to be displaced. Those compounds in which (R^2) is a group other than hydrogen were shown to react more readily than the comparable unsubstituted compounds, irrespective of the polar nature of the substituent. This seems to imply that the substituent (R^2) is needed to hold the dyestuff in the more favourable conformation (13) rather than in the alternative conformation (14; R^1=H or NHCOMe).



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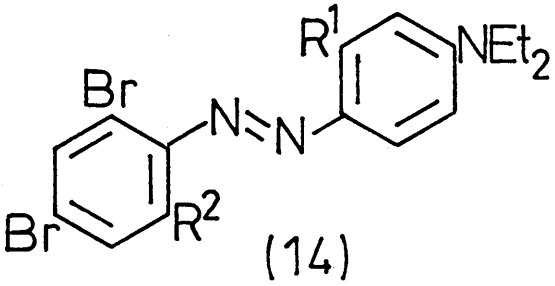


(14)

It is interesting to note that a substituent other than hydrogen at R^2 in (13) was not found to be necessary in the copper-promoted substitution reactions of the dyestuffs (13) with phosphines, reported by Allen et al[1].

The major difference between the 'simple' azodyestuffs (11; R=H or NHCOMe) used in the present study and (13)

[the reaction of which is catalysed by copper (II) acetate] is that no other substituent is found in the aryl ring bearing the bromine atom to be displaced. Thus, it seems that in order for copper (II) acetate to catalyse such substitution reactions, the ring carrying the halogen atom needs substituents at the para- and/or ortho´- positions.

3.3.2 Initial Rate Studies

The initial study commenced by heating together in ethanol, the Schiff's base (9) with the preformed nickel (II) - phosphine complex (15; R=Ph or Bu) in a 1:1 molar ratio. The reaction was carried out under reflux for a period of 24 hours. The major problem encountered with this system was the insolubility of the preformed nickel (II) phosphine complex (15; R=Ph or Bu) in refluxing ethanol.

$$\left[(R_3P)_2NiBr_2 \right] \text{ ——— (15)}$$

To create a more homogenous system, it was decided to revert back to the original precursors, i.e. this initially involved the Schiff's base (9), with triphenylphosphine and nickel (II) bromide in ethanol in the ratios of 1:2:0.2, respectively. It was hoped that the progress of the reaction could be followed either (i) fluorometrically, or (II) spectrophotometrically. However, it was found that none of the Schiff's base phosphonium salts fluoresced and that the wavelength separation between the U.V. - visible absorption maxima of the parent Schiff's base and its

salt was negligible.

Therefore, it was decided to explore alternative approaches for the study of the Schiff's base system. Eventually, two techniques were employed for both the Schiff's base and azodyestuff templates, which allowed the progress of the reactions to be monitored:

(a) For Schiff's base templates - Detection of the phosphonium salt was easily achieved using a conductiometric method, since the ionic product is generated from a largely non-conducting solution.

(b) For the azodyestuff templates - Detection of the phosphonium salt was achieved using a spectrophotometric technique in which the absorption of the salt in the visible region was monitored. This was only viable when the visible absorption maxima of the salts and the related templates were separated by at least 60 nanometers (nm.). For cases where separation of the absorption maxima was <60 nm., the progress of the reaction was followed conductiometrically.

3.3.3 Factors Affecting the Overall Isolated Yield Of Phosphonium Salts

In order to justify a detailed kinetic study, it was necessary to demonstrate that the template reactions proceeded in > 90% yeild, i.e. that no significant side reactions interfered with the formation of the phosphonium salt product.

It is known that the template-assisted phosphonium salt formation reactions proceed in both ethanol and

acetonitrile[1]. However, isolated yields under various conditions had not been fully established in earlier work. Hence, in the following study the influence of changes in solvent, quantities of reactants, temperature and changes in the nature of the Schiff's base substrate and catalyst, on the overall isolated yield of phosphonium salt were evaluated for reactions carried out over a 24 hour period. The results are summarised in Table 3.1, which also includes the results of a limited study of two o-haloaryl dyestuff templates.

Table 3.1 Overall Yield Study

		QUANTITIES USED IN MOLAR RATIOS					
No.	SOLVENT	BR-SCHIFFS BASE	Ph_3P	$NiBr_2$	YIELD (g)	%YIELD	TEMP. (°C)
1	EtOH	1	3	0.2	0.94	99	80
2	CH_3CN	1	3	0.2	0.31	33	82
3	MeOH	1	3	0.2	0.20	21	64
4	$CHCl_3$	1	3	0.5	0.03	6	61
5	95%EtOH/ 5% H_2O	1	3	0.2	0.13	34	80
6	EtOH	1	3	0.2	0.85	90	70*
7	EtOH	1	3	0.2	0.33	35	60*
8	EtOH	1	2	0.2	0.90	95	80
9	EtOH	1	2	0.2	0.60	63	70*
10	EtOH	1[a]	3	0.2	0.50	49	80
11	EtOH	1[a]	2	0.2	0.21	21	80
12	EtOH	1[b]	3	0.2	1.03	100	80
13	EtOH[c]	1	3	0.2	0.94	99	80

NO.	SOLVENT	BR-SCHIFFS BASE	Ph_3P	$NiBr_2$	YIELD (g)	%YIELD	TEMP. (°C)
14	EtOH[c]	1	3	0.2[d]	0.82	86	80
15	EtOH[c]	1	3	0.2[e]	0.96	100	80
16	EtOH	1	2	0.5[f]	0.10[g]	18	80
17	EtOH[c]	1[h]	3	0.2	1.01	99	80
18	EtOH[c]	1[i]	3	0.2	0.90	100	80

Reaction time 24 hours.

* Temperatures controlled using a thermostatted water bath

a Ortho-chloro-Schiff's Base

b Ortho-iodo-Schiff's Base

c 'Super Dry' Ethanol

d Nickel (II) Chloride

e Nickel (II) Iodide

f Cobalt (II) Bromide

g Extended reaction time (72 hours)

h Ortho-bromodiarylazodyestuff (type II)

i Ortho-bromodiarylazodyestuff (type III)

The template reaction proceeds in all the examples above but to varying extents. The following observations may be made:-

(i) It can be seen that the presence of an extra mole of phosphine results in a higher yield of product. (c.f. reactions No.1 vs No.8, No.6 vs No.9 and No.10 vs No.11).

(ii) As the temperature decreases so does the yield. (c.f. reactions No.1 vs No.7 and No.6 vs No.7).

(iii) The nature of the halogen in the ortho- position on the Schiff's Base template has a considerable effect on the overall yield of the reaction. (c.f. reactions No.1 vs No.10 and No.8 vs No.11).

(iv) In earlier work, it was observed that cobalt (II) bromide catalysed the template reaction. It is evident from the table that even after prolonged heating over 72 hours, the amount of product isolated is minimal with respect to the nickel (II) bromide catalysed reaction (c.f. reaction No.1 vs No.16).

(v) The yield is also dependant on the solvent used. (c.f. reactions No.1 vs Nos. 2, 3, 4 and 5).

(vi) In (v), the effect which the solvent has on the overall yield is clear. However, the yield of product remained the same for the template reaction carried out in either 'Super Dry' or 'Bench' ethanol, even though the latter can contain on average up to 1% of water (c.f. reaction No.1 vs No.13). A more drastic change in the final yield occurred when a 5% aqueous ethanolic solution was used in preference to either of the latter solvents (c.f. reaction No.1 vs No.5), therefore indicating that the water content of the ethanol is important. As a result of this observation, all subsequent kinetic studies were carried out using 'Super Dry' ethanol.

(vii) By comparison, the overall yields of the corresponding reactions of the azodyestuffs are similar to those of the Schiff's base template systems (c.f. reaction No.13 vs Nos. 17 and 18).

3.4 A KINETIC STUDY OF THE NICKEL (II) CATALYSED REACTIONS OF ORTHO-HALOARYL SCHIFF'S BASE TEMPLATES WITH TERTIARY PHOSPHINES

In the light of the preceding study of overall yields of phosphonium salts, the following conditions were employed in the subsequent kinetic studies:- The 'standard' ratio of the Schiff's base: phosphine: nickel (II) halide catalyst used was 1:3:0.2, respectively. All the reactions were carried out in refluxing 'Super Dry' ethanol, on a sand bath under a nitrogen atmosphere for a period of 24 hours. Sampling was achieved by inserting a 1 ml pipette down the middle of the condenser, transferring the aliquot to a 10 ml volumetric flask and diluting the sample to the mark with cold 'Super Dry' ethanol. Detection of the phosphonium salt using a conductiometric method (a Wayne-Kerr conductance bridge) was easily achieved. It was also essential before taking any readings to submerge the samples in a thermostatically - controlled water bath (25°C) and allow them to equilibrate since it is known that a one degree change in temperature can affect the conductance of a solution by as much as 3-5% (per degree).

In order to evaluate the effect which each reactant has on the overall rate of the reaction, several mini-investigations were undertaken.

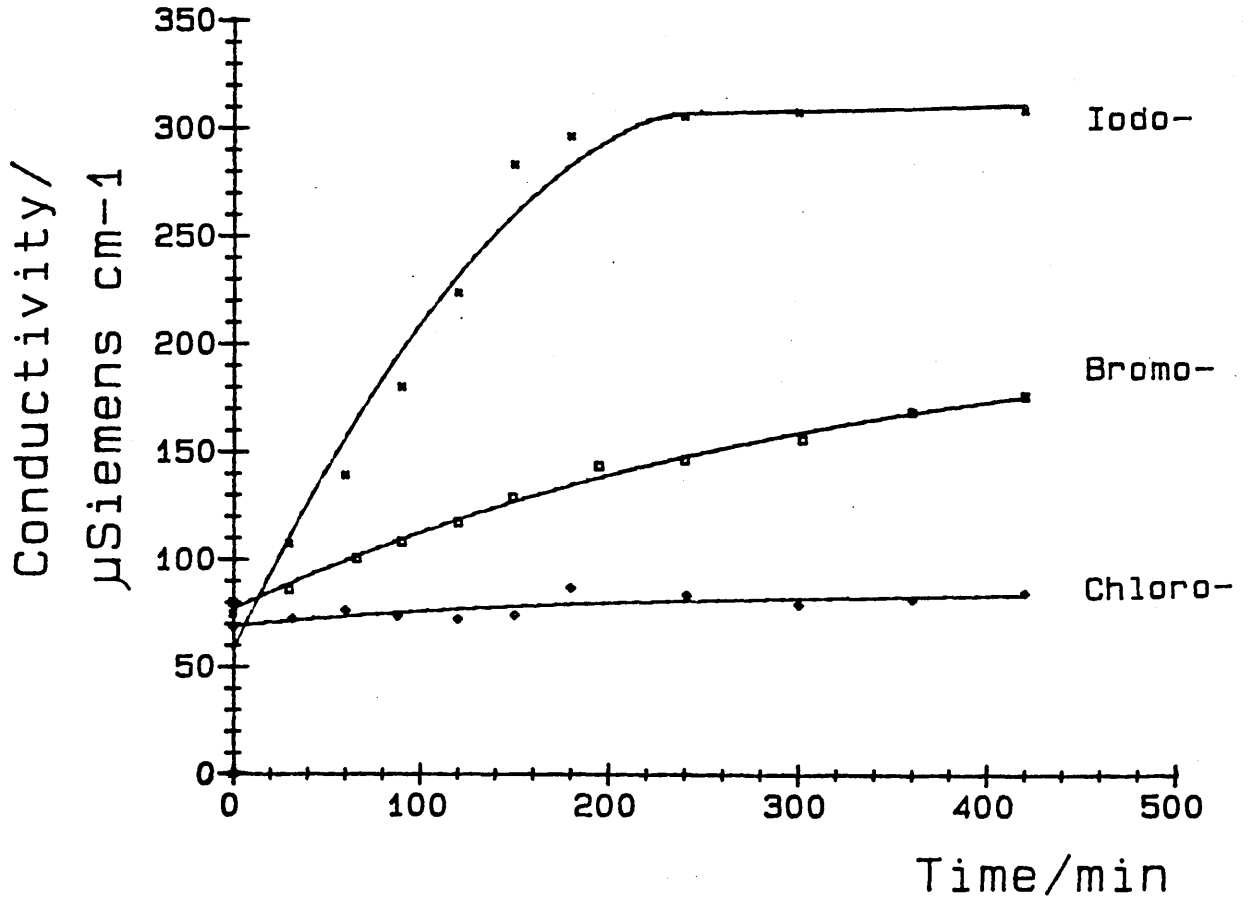
3.4.1 Dependence of Rate on Each Reactant

(A) Dependence on the Halogen Replaced by Phosphorus

The aim of this study was to observe the effect on the rate of the reaction of changing the identity of the

imino-halogen whilst keeping the nickel (II) catalyst and phosphine concentrations constant.

When graphs of conductivity [measured in micro-siemens per centimetre (μScm^{-1})] against time were plotted (Graph 3.1) the first noticeable feature was that the range of conductivities over which the reaction of the ortho-iodo-Schiff's base-substrate had to be followed was much larger than for the o-bromo-Schiff's base, which in turn was larger than for the o-chloro-Schiff's base. This difference in conductivities is not directly relevant in the determination of relative rates of reaction; the latter requires a consideration of the time taken to reach any given extent of completion. Since the phosphonium cation being produced is the same in all the reactions, then the reason for the increased conductivities must in some way depend on the nature of the anion. This discrepancy can be explained by taking the solvation of the ions into account. Solvent molecules cluster around the ion and increase its effective size. Small ions are the source of stronger electric fields than large ions (the electric field at the surface of a sphere of radius R is proportional to ze/R^2, where ze is the charge on an ion) and therefore, the solvation is more extensive in the case of small ions (Table 3.2)[5]. They have larger solvated radii than larger ions, lower drift velocities (a result of frictional forces opposing an ion moving through a potential gradient), and therefore lower conductivities.


Conductivity/
µSiemens cm-1
350
300
250
200
150
100
50
0
0
100
200
300
400
500
Time/min
Iodo-
Bromo-
Chloro-

Graph 3.2

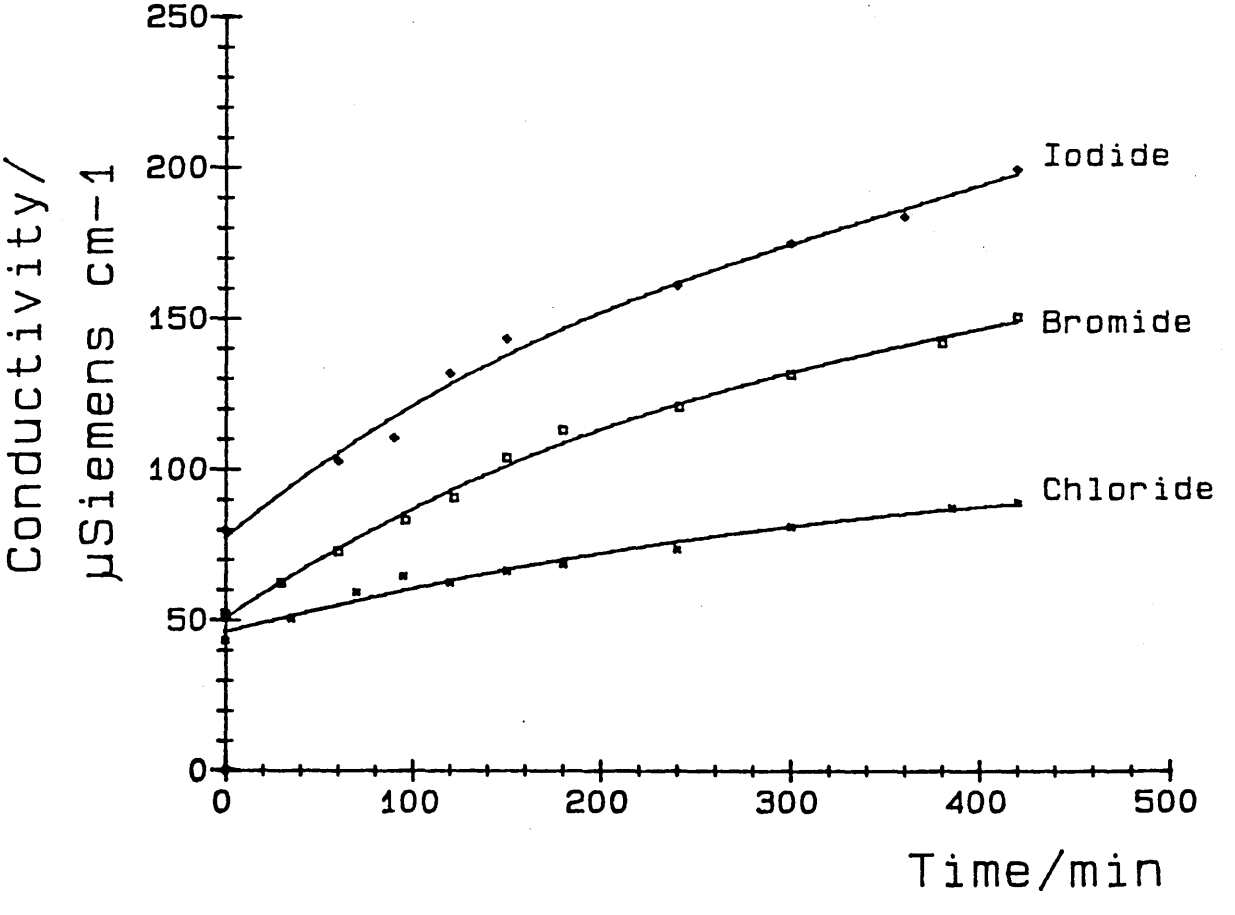

Conductivity/
µSiemens cm-1
250
200
150
100
50
0
0
100
200
300
400
500
Time/min
Iodide
Bromide
Chloride

Table 3.2 Ionic Radii/nm

Ion	Radius/nm
Cl	1.81
Br	1.95
I	2.16

From this initial study, no rate constants were obtainable, but it appears from a brief consideration of initial slopes that the rate of the reaction with respect to the o-halosubstituent is in the order of I>Br>Cl.

(B) Dependence on the Halogen Present in the Nickel (II) Catalyst

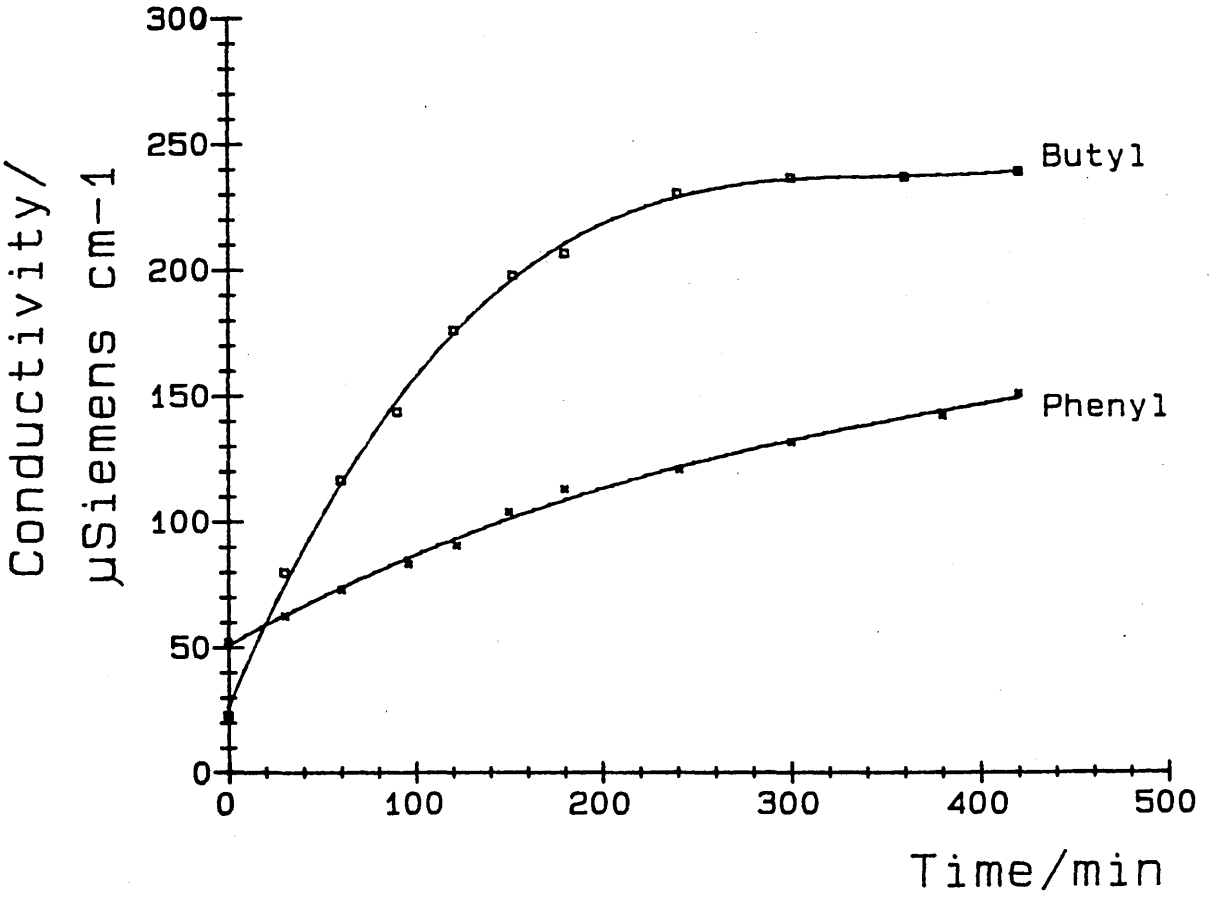
In this study, the aim was to change the identity of the nickel (II) halide catalyst, whilst keeping the halo-Schiff's base template and phosphine concentrations constant.

It can be seen from the conductivity/time plots (Graph 3.2) that the initial slopes, allowing for experimental error, are approximately the same. This would suggest, that the identity of the halide in the nickel (II) catalyst is unimportant.

(C) Dependence on the Nature of the Phosphine

The aim of this study was to investigate the effect of changing the nature of the phosphine whilst keeping the concentrations of the nickel (II) catalyst and o-haloarylimine template constant.

Graph 3.3



From the plot of conductivity against time (Graph 3.3) it seems that the rate of reaction is faster for tributylphosphine than for triphenylphosphine. In terms of relative rates, the reaction with tributylphosphine is approximately three times faster than that with triphenylphosphine. This difference in the initial slopes can be accounted for in terms of:-

(i) the difference in the donor character of the phosphine: Bu_3P > Ph_3P (i.e. the effect of alkyl vs aryl substituents).

(ii) steric hindrance, i.e. three bulky phenyl groups crowded into the reaction site as opposed to the more floppy, less rigid butyl groups.

(D) Dependence on the Concentration of the Phosphine

The above preliminary investigations have given an insight into how the nature of each substrate affects the rate of the reaction, on a purely qualitative basis. The next stage of the study required a more critical view of the reaction involving studies of the effects of changes in the concentration of each reactant, whilst keeping the concentrations of the other two constant.

In this study the ratio of the concentrations of o-haloaryl-Schiff's base to nickel (II) bromide catalyst was kept constant, i.e. 1:0.2 moles respectively, whilst the concentration of the phosphine was changed from 1:2:3:4:5:10 and 15 mole equivalents respectively.

From the conductivity - time data obtained, it could be assumed that the rate of the reaction is unaltered once a minimum amount of phosphine is present (i.e. greater than a 1:5 ratio). The initial slopes of the plots when Schiff's base:phosphine concentrations were 1:5, 1:10 and 1:15 respectively were all the same, as opposed to those observed when the concentration ratios are below 1:4 moles respectively. A slight divergence of the plot observed when Schiff's base:phosphine concentration is 1:15 could be due to the problems experienced with the phosphine crystallising out of solution on quenching the sample to its ten-fold dilution.

(E) Dependence on the Concentration of the Schiff's Base

In this study, the ratio of the concentration of phosphine to nickel (II) bromide catalyst was kept constant i.e. 3:0.2 moles respectively, whilst the concentration of the Schiff's base was changed from 0.5:1:2 and 4 mole equivalents respectively. From conductivity - time plots, it appears that the rate of the reaction increases as the concentration of the imine increases.

(F) Dependence on the Change in Concentration of the Catalyst

In this study, the ratio of the concentrations of Schiff's base to phosphine were kept constant, i.e. 1:3 moles respectively, whilst the concentration of the nickel (II) bromide catalyst was changed from 0.1:0.2:0.4 and 0.8 moles respectively.

In these studies, it might be assumed that for an increase in the concentration of catalyst, an increase in the rate of formation of phosphonium salt would result. However, the initial slopes of all the conductivity - time plots were similar (allowing for experimental error), therefore implying essentially the same rate of reaction. However, later studies [section 3.4.2(C)] conducted over a 24 hour period revealed the expected increase in rate as the concentration of catalyst increased.

In the next section, the kinetic order with respect to each reactant and the overall order of the reaction will be assessed.

3.4.2 Order of Reaction

In order to determine the kinetic order of the reaction from the conductivity data, it was necessary to plot graphs of various integrated forms of the rate equations in order to see which gave a straight line.

Initially, it was found that by plotting ln (G_∞ - Gt) against time [where G_∞ is equal to the conductivity at infinite time, (i.e. 24 hours) and Gt is equal to the conductivity at time t] all the plots were non-linear, signifying that none of the reactions obeyed overall first order kinetics.

On plotting $1/(G_\infty - Gt)$ against time, it was observed that linear plots were encountered at low extents of reaction (i.e. below 150 min), but then curvature developed. This behaviour is consistent with a 'second order unequal' rate law for the reaction. Such behaviour is observed in second order reactions where the concentrations of reactants at the beginning of the reaction are unequal. At low extents of reaction, behaviour follows second order kinetics, but as the reaction progresses, the concentration of one of the reactants becomes significantly reduced compared with the other until the second reactant is effectively present in excess. At this stage, the reaction exhibits pseudo first order rate behaviour.

Having ascertained that the reaction could be 'second order unequal', for a straight line graph covering all of the points was required, it would be necessary to plot the following terms:-

$$\ln \left[\frac{[SB]_0[R_3P]}{[SB]\ [R_3P]_0} \right] \text{ against time}$$

where $[SB]_0$ is the initial concentration of Schiff's base

$[R_3P]_0$ is the concentration of tertiary phosphine

$[SB]$ is the concentration of Schiff's base at time t

$[R_3P]$ is the concentration of tertiary phosphine at time t

This plot would be prohibitively complicated since the conductiometric data obtained only relates to the appearance of the phosphonium salt product and not to the disappearance of the two reactants. However, a way around this problem is to keep the concentration of two of the reactants constant, whilst altering the concentration of the third.

For this study the reactants chosen were the Schiff's base (9) triphenylphosphine and nickel (II) bromide as the catalyst, in varying ratios.

An important point to note is that the rate constants obtained from this study, and from subsequent studies undertaken are those for the pseudo - first order plots (k_1') and not the genuine first - order rate constants (k_1). Such rate constants only allow comparisons of relative rates to be made.

(A) The Order with Respect to the Phosphine

These reactions were carried out under pseudo first order conditions and the following data were obtained

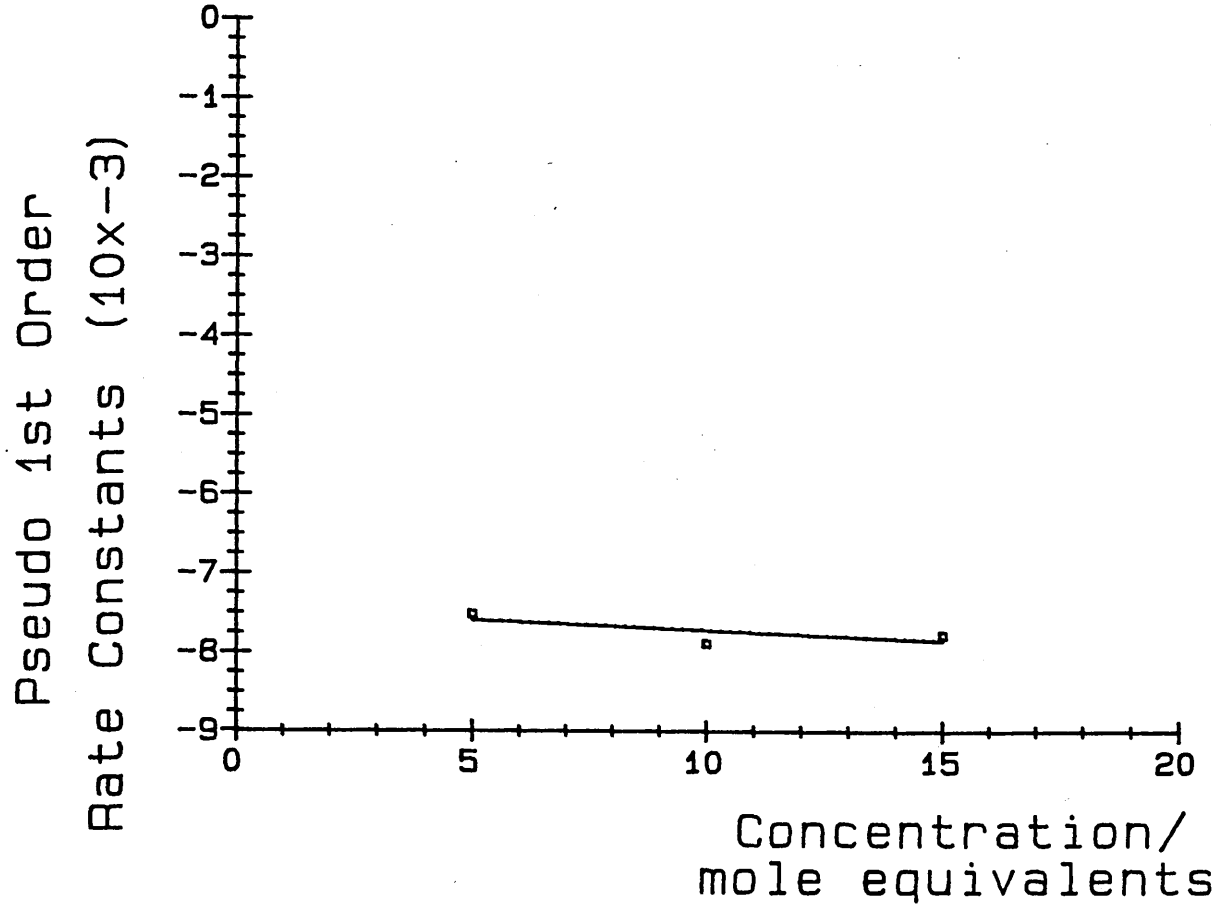
from the plots of ln (G_∞ - Gt) against time (min).

Table 3.3

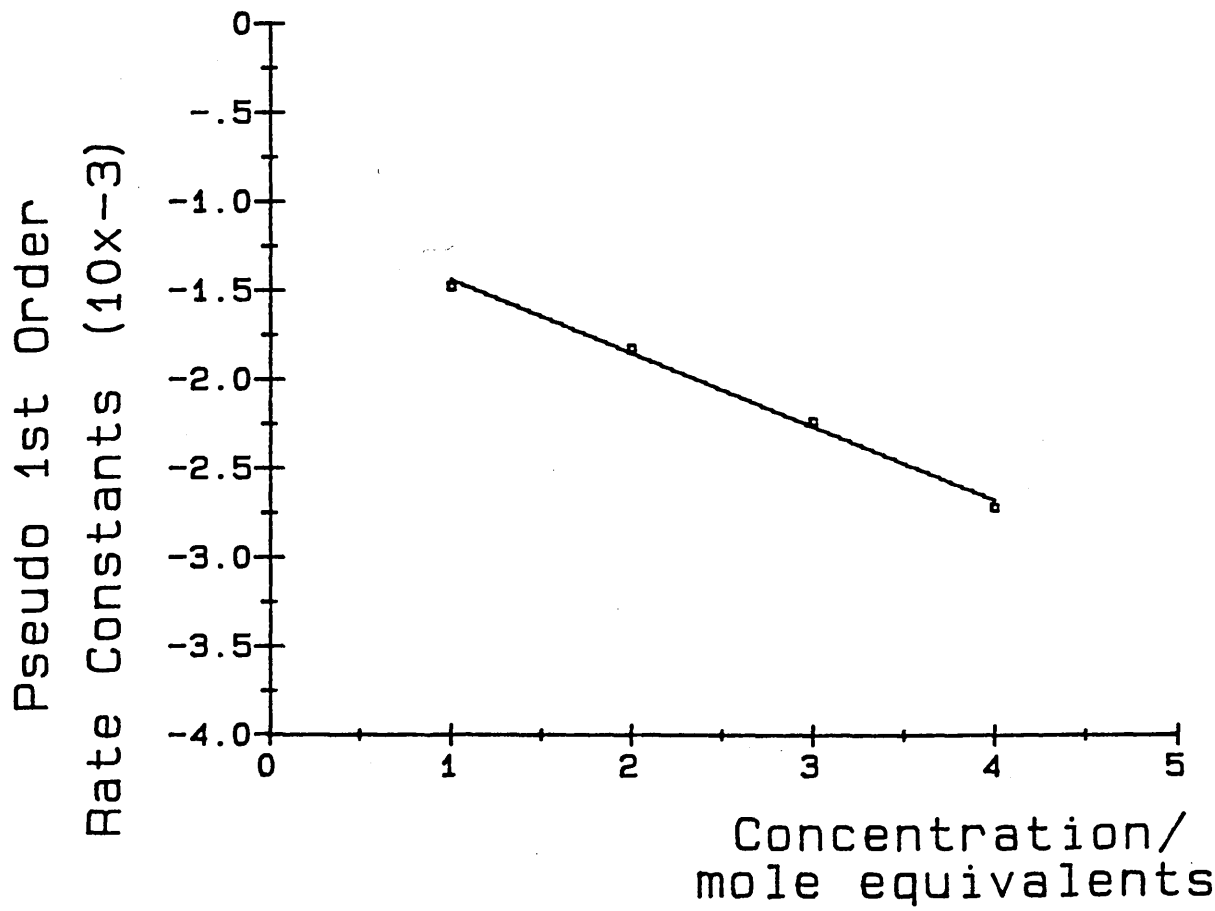
Mole Ratio of Phosphine:Imine (n) (1) :Catalyst (0.2)	Gradient ($\times 10^{-3}$)	Correlation Coefficient
n=1	-1.4786	0.9986
n=2	-1.8356	0.9890
n=3	-2.2324	0.9974
n=4	-2.7162	0.9905
n=5	-7.5238	0.9981
n=10	-7.8889	0.9695
n=15*	-7.7768	0.9845

* The last three points on this plot were disregarded

From the Table 3.3 and Graph 3.4, it can be seen that on increasing the phosphine to Schiff's base ratio from 5:1 to 15:1, there is no apparent change in the rate of the reaction. However, there is a marked difference where, for example, the ratio is 4:1. Therefore, from the information above, it could be assumed that the concentration of phosphine has no direct effect on the rate of the reaction, provided that there is an excess of phosphine present initially, i.e. a minimum of 5:1 excess. Therefore, it could be assumed that the order with respect to the phosphine is zero under such conditions, i.e. $[PR_3]^0$. Nevertheless, that the phosphine contributes in some measure to the overall rate equation at lower concentrations, is shown by Graph 3.5. This demonstrates that at lower


Pseudo 1st Order
Rate Constants (10x-3)
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
0
5
10
15
20
Concentration/
mole equivalents

Graph 3.5


Pseudo 1st Order
Rate Constants (10x-3)
0
-.5
-1.0
-1.5
-2.0
-2.5
-3.0
-3.5
-4.0
0
1
2
3
4
5
Concentration/
mole equivalents

concentrations of phosphine, a first order rate dependence is observed, i.e. $[PR_3]^1$.

(B) The Order with Respect to the Schiff's Base

The following data were obtained from the plots of $\ln(G_\infty - Gt)$ against time.

Table 3.4

Mole Ratio of Imine:Phosphine (n) (3) :Catalyst (0.2)	Gradient ($x10^{-3}$)	Correlation Coefficient
n=0.5	-2.7089	0.9981
n=1	-2.2324	0.9974
n=2	-1.9227	0.9995
n=4	-1.7300	0.9979

From Table 3.4 it can be observed that as the ratio of Schiff's base to phosphine increases, the rate of the reaction appears to decrease. If there is more Schiff's base present in the reaction mixture one might assume that the rate would almost certainly increase. However it does not appear to behave in this way. Two possible explanations of this behaviour are (a) competition between the imino-nitrogen and the phosphine for coordination to the nickel (II) catalyst and (b) that the mole ratios between both the Schiff's base and phosphine [the two competing species in (a)] vary from between a six-fold excess of phosphine to Schiff's base (3:0.5) in the first

reaction to a reversal of this situation in the final reaction (3:4). However, a plot of the data obtained in the early stages of each reaction (Table 3.5) (up to 150 mins of 24 hours) revealed a first order dependence of the rate on the concentration of Schiff's base, i.e. [Schiff's base]^{1} (Graph 3.6).

Table 3.5

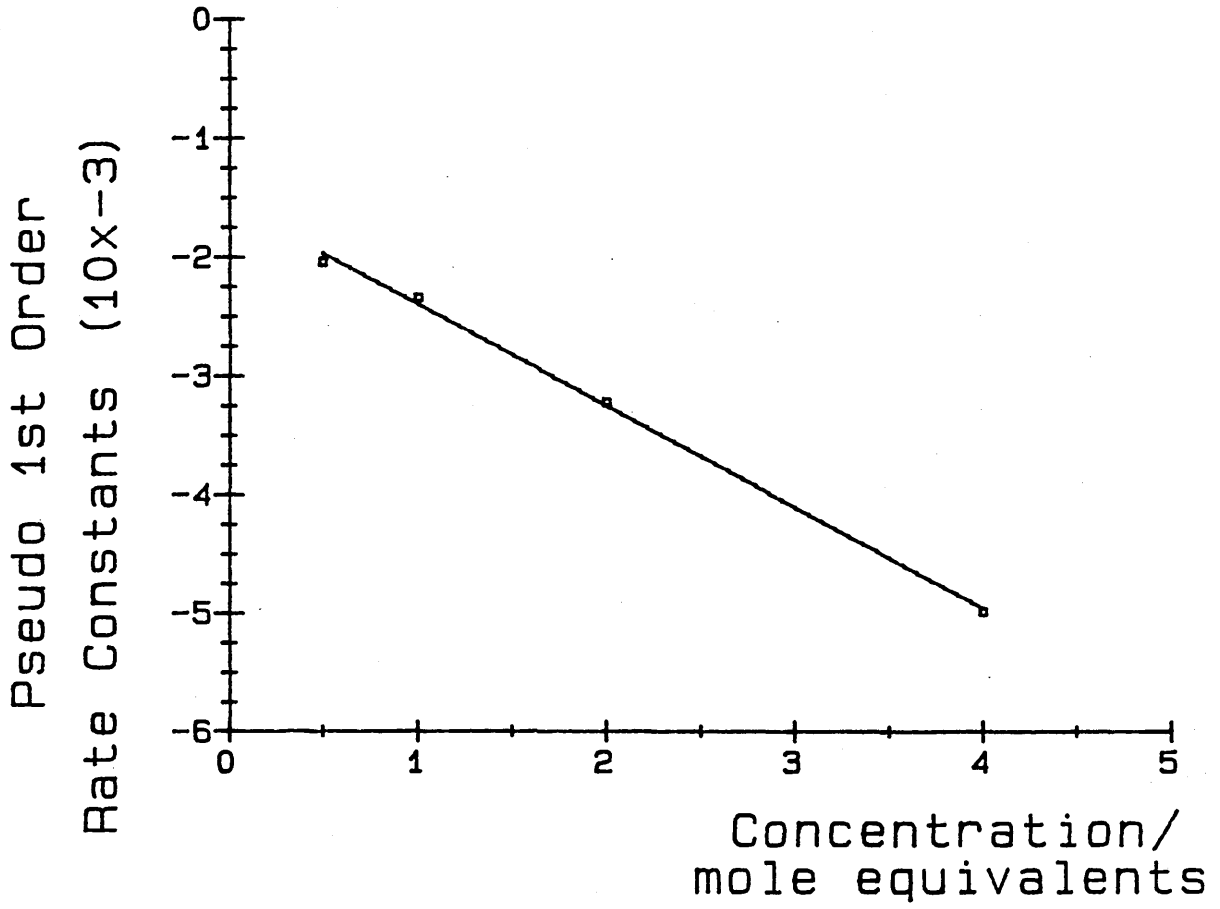
Mole Ratio of Imine:Phosphine (n) (3) :Catalyst (0.2)	Gradient ($x10^{-3}$)	Correlation Coefficient
n=0.5	-2.0450	0.9978
n=1	-2.3461	0.9903
n=2	-3.2245	0.9991
n=4	-4.9875	0.9974

(C) The Order with Respect to the Catalyst Concentration

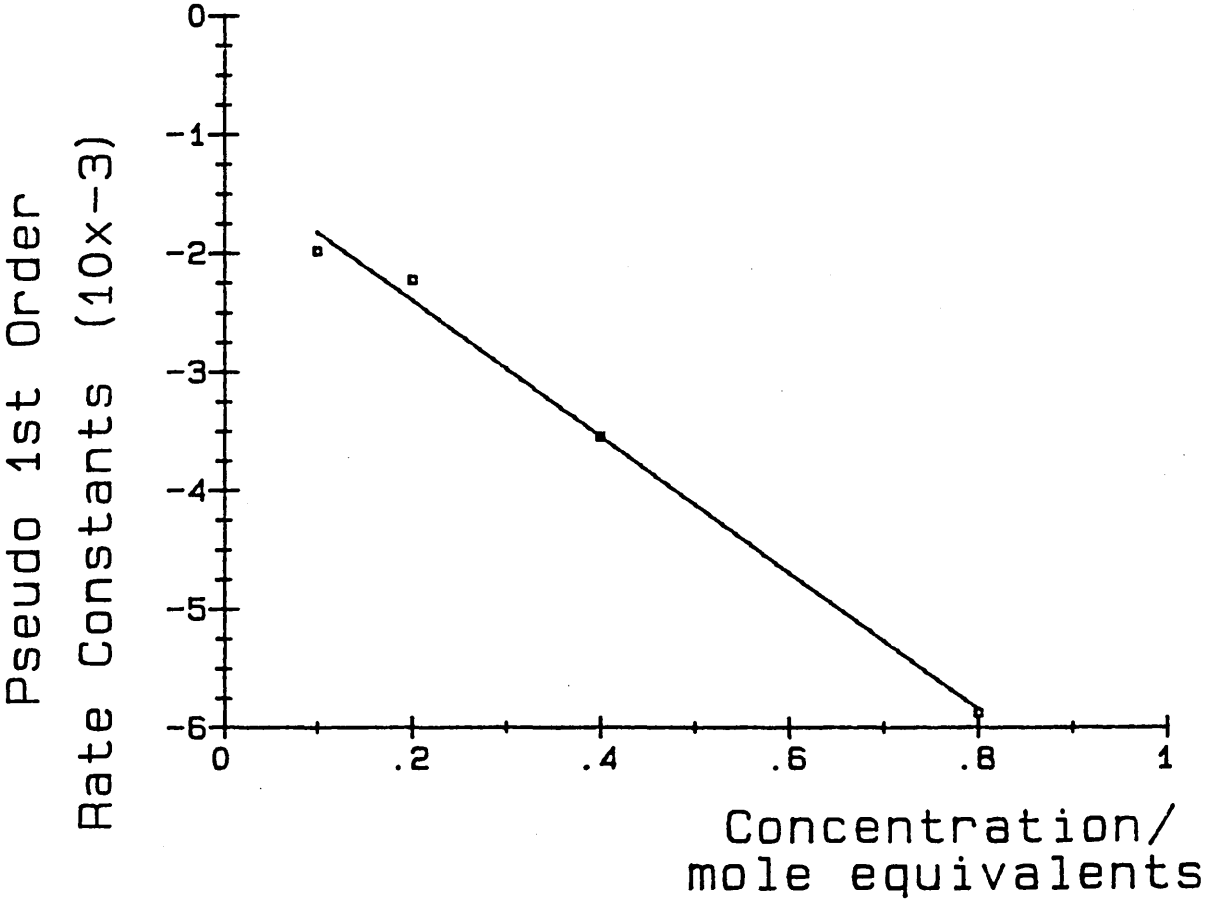
The following data were obtained from the plots of $\ln(G_{\infty} - Gt)$ against time.

Table 3.6

Mole Ratio of Catalyst:Imine (n) (1) :Phosphine (3)	Gradient ($x10^{-3}$)	Correlation Coefficient
n=0.2	-1.9870	0.9981
n=0.2	-2.2324	0.9974
n=0.4	-3.5534	0.9983
n=0.8	-5.8783	0.9979


Pseudo 1st Order
Rate Constants (10x-3)
0
-1
-2
-3
-4
-5
-6
0
1
2
3
4
5
Concentration/
mole equivalents

Graph 3.7


Pseudo 1st Order
Rate Constants (10x-3)
0
-1
-2
-3
-4
-5
-6
0
.2
.4
.6
.8
1
Concentration/
mole equivalents

From these results (Table 3.6), it can be observed that as the mole ratio of nickel (II) bromide increases then so does the rate of the reaction (Graph 3.7). This finding is consistent with earlier qualitative studies (Allen et al[1]). From the data collected, the order with respect to the catalyst is first order under the reaction conditions, i.e. [catalyst]^1.

3.4.3 Summary

After completing the kinetic studies involving Schiff's base substrates, it is of interest to evaluate the findings in terms of an initial rate law. This can be expressed in the form of a third order rate law, providing that the ratio of the concentration of phosphine: Schiff's base is below 4:1.

i.e. $\text{Rate} \propto \frac{d[P^+]}{dt} \propto [S.B.]^1 \ [R_3P]^1 \ [cat]^1$

$\therefore \quad \text{Rate} = k_3[S.B.]^1[R_3P]^1[cat]^1$

where k_3 = rate constant for the third order rate law

$[S.B.]$ = concentration of Schiff's base

$[R_3P]$ = concentration of phosphine

$[cat]$ = concentration of catalyst

$\frac{d[P^+]}{dt}$ = rate of appearance of phosphonium salt

A second order rate equation is valid if the phosphine concentration increases above a 5:1 ratio. This second order rate law can be expressed as;

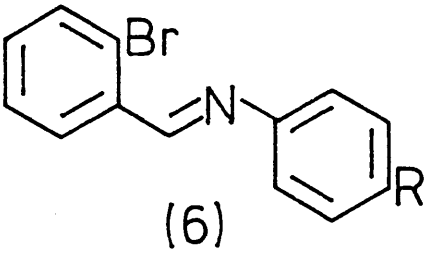
$$\frac{d[P^+]}{dt} \alpha [S.B.]^1[cat]^1$$

$$\therefore \text{ Rate} = k_2 [S.B.]^1 [cat]^1$$

where k_2= rate constant for the second order rate law

3.4.4 The Electronic Effects of Para-Substituents in the Remote Aryl Ring in Ortho-Haloaryl-Schiff's Base Templates

Having established that the imine is kinetically significant, it was of interest to study the effects on the rate of the reaction of varying electron density at the imino-nitrogen. For this purpose, the reactions of a range of Schiff's bases (6; R=H, Me, Br, OH, CN, NO_2, CO_2Et, NHPh or NEt_2), bearing a p-substituent in the remote aryl ring, were studied.

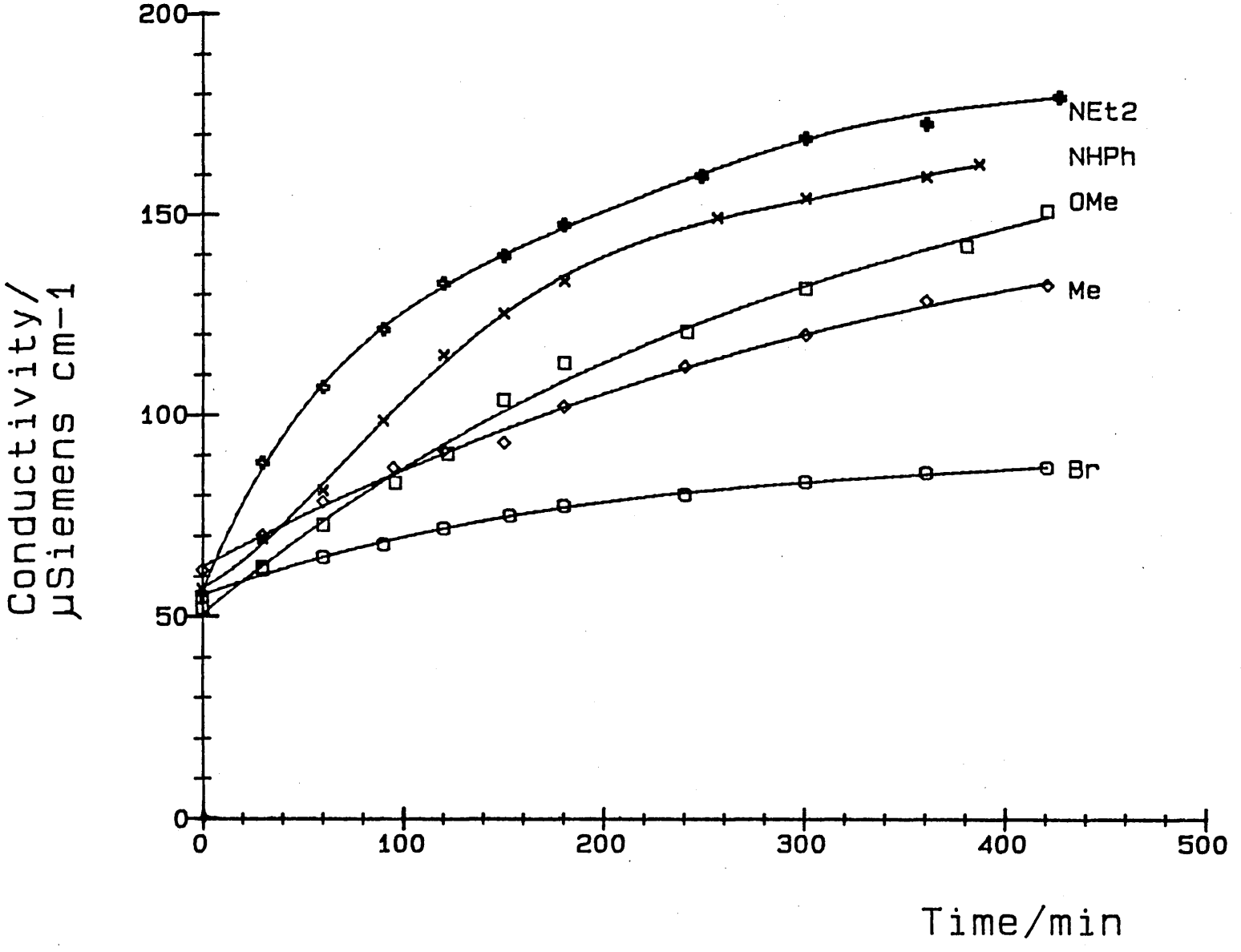


(6)

Two effects were observed:

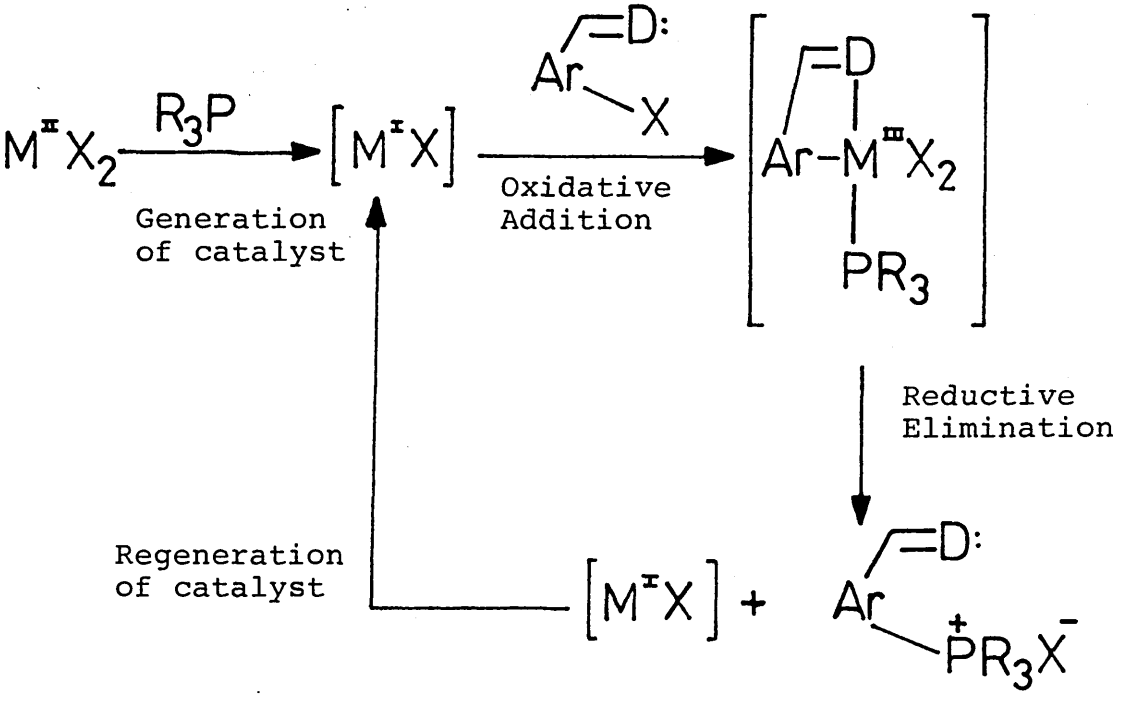
(a) Whilst undertaking a relative rate study on the reactions of the above range of Schiff's bases, a plot of conductivity against time (Graph 3.8) revealed that the more negative the Hammet σp value i.e. the more electron-donating the p-substituent) the faster the reaction occurred. In contrast, the more positive the σp value

Graph 3.8


Conductivity/
µSiemens cm-1
200
150
100
50
0
0
100
200
300
400
500
Time/min
NEt2
NHPh
OMe
Me
Br

the slower the reaction. The fact that electron-donating substituents increase the rate of the reaction reinforces the basic assumption (Scheme 1) that the imino-nitrogen must at a critical stage donate its lone pair of electrons to the incoming nickel-phosphine complex and that this process is strengthened by the increased electron density around the nitrogen atom.

(b) In two cases, for (6; R=CN(σp 0.6)) and (6; R=NO_2 (σp 0.78)) the substitution reaction failed to take place.



(Scheme 1)

During this investigation, an attempt to plot σp values against the rate constants obtained from the reactions of the Schiff's bases (6) that were successful failed to show any Hammett type relationship. However a relationship was established between the σp values and ^{31}P n.m.r. chemical shifts (Graph 3.9). Although the chemical shifts only cover a range of 1 ppm the relationship is significant having a correlation coefficient of 0.9950 (Table 3.7).

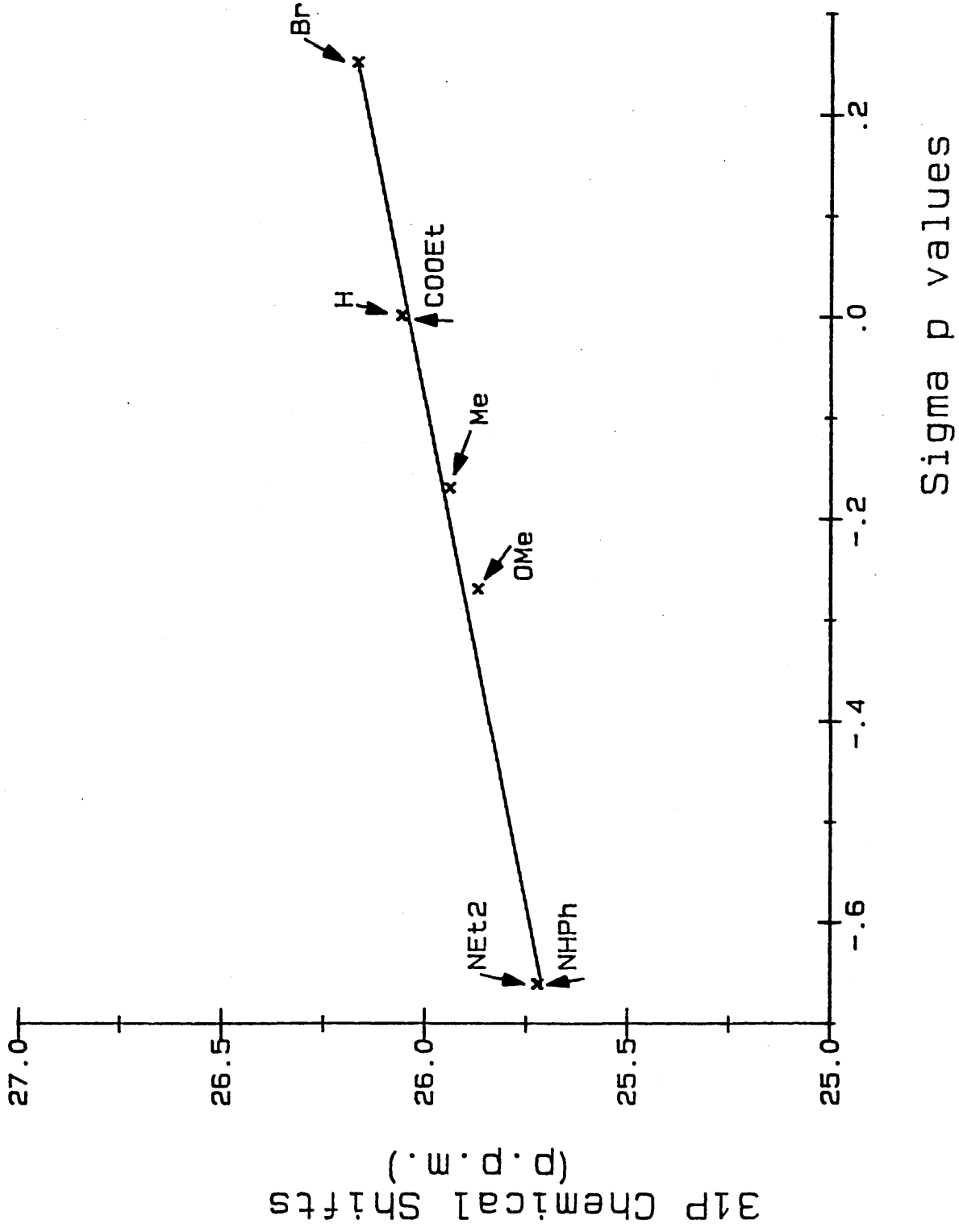
Table 3.7

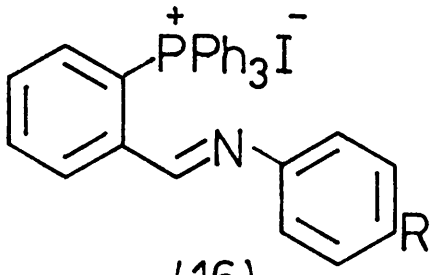
^{31}P Nmr Chemical Shift Data for Substituted Schiff's Base Phosphonium Salts (16) in Deuteriochloroform

Compound	σp	$\delta^{31}P$/p.p.m.
NO_2	0.78	-
CN	0.60	-
Br	0.25	26.17
CO_2Et	0.00	26.06
H	0.00	26.05
Me	-0.17	25.94
OMe	-0.27	25.87
OH	-0.37	26.56*
NHPh	-0.66	25.72
NEt_2	-0.66	25.72

* Not soluble in $CDCl_3$, soluble in Trifluoroaceticacid/D_2O

Graph 3.9


Br
H
COOEt
Me
OMe
NEt2
NHPh
27.0
26.5
26.0
25.5
25.0
-.6
-.4
-.2
.0
.2
31P Chemical Shifts
(p.p.m.)
Sigma p values



(16)

The Hammett equation[6] has been applied successfully to a number of reactions involving organophosphorus compounds. Other workers[7] have reported Hammett relationships for a number of substituted phenylphosphonic acids. In particular, Freedman and his co-workers[8,9] have investigated substituent effects in ^{31}P n.m.r. spectroscopy and have obtained linear correlations between the ^{31}P chemical shifts of a number of substituted phenylphosphonic acid derivatives and the corresponding σm or σp constants. Mellor[10], has achieved similar results whilst plotting the ^{31}P chemical shifts of substituted phenylphosphonates against Hammett σm and σp substituent constants.

3.4.5 Further Consideration of the Effects of the Ortho-Halogen Displaced on the Rate of the Substitution Reaction

In an earlier qualitative study[1], it was shown that the relative rates for the reactions of the ortho-halo-Schiff's bases followed the trend I>Br>Cl. This trend is opposite to that observed in nucleophilic aromatic substitution processes (e.g. nucleophilic substitution of 2,4-dinitrohalobenzenes) where the order in Cl>Br>I[11].

A quantitative study using the Schiff's bases (5; X=Cl, Br or I) (1 mole): triphenylphosphine (3 moles): nickel (II) bromide (0.2 moles) confirmed the earlier qualitative observation. It has been possible to obtain a straight line for the first six data points (Table 3.8) of each of the reactions of the o-haloaryl Schiff's bases by plotting ln (G_∞ - Gt) against time, i.e. a pseudo first order plot for the initial period of the reaction.

Table 3.8

Table of ln (G_∞ - Gt) values

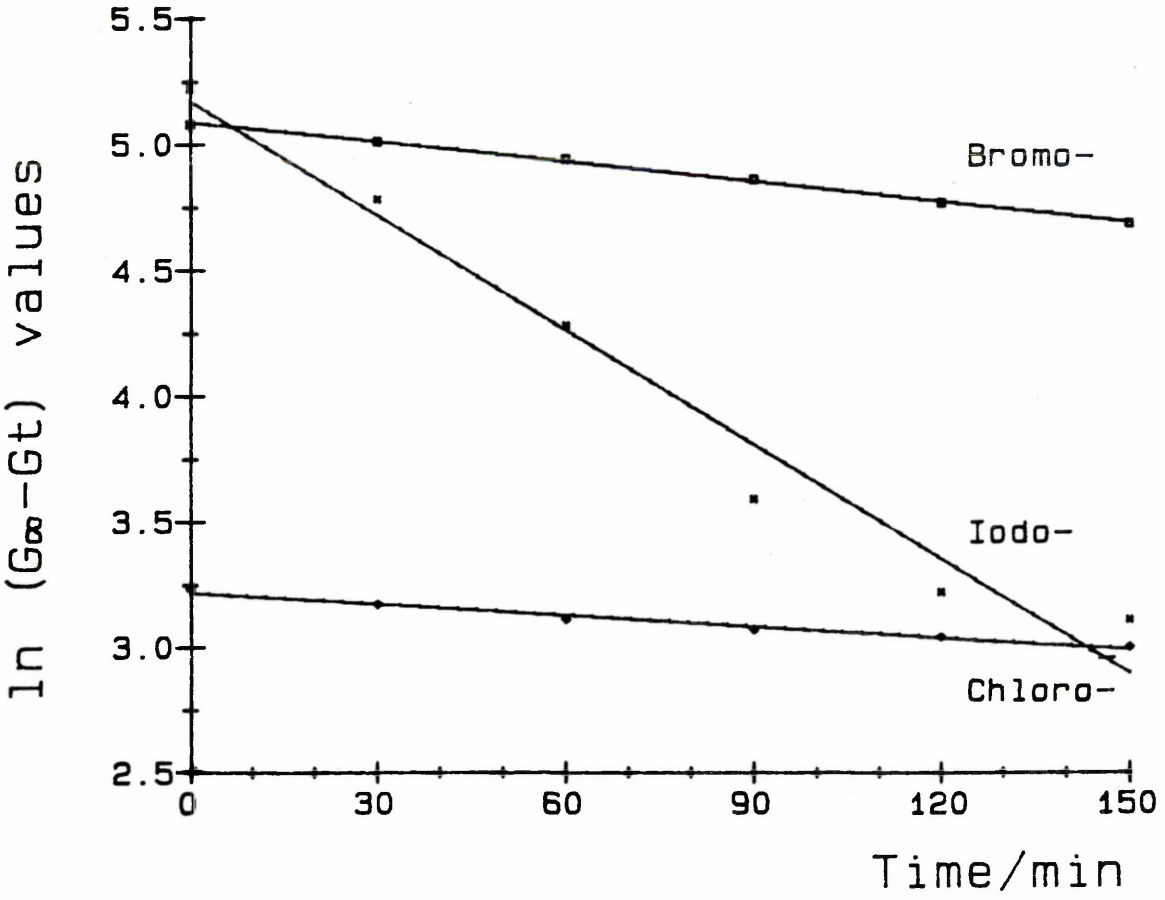
t/min	Chloro-	Bromo-	Iodo-
0	3.23	5.08	5.22
30	3.17	5.01	4.78
60	3.11	4.94	4.28
90	3.07	4.86	3.59
120	3.04	4.77	3.22
150	3.00	4.69	3.11

A comparison of the gradients (i.e. the pseudo first order rate constants) of the three straight lines (Graph 3.10) reveals the relative rates of reaction of the three ortho-haloaryl Schiff's bases. It is found that the gradients, and hence the relative rates of reaction of the Schiff's bases vary widely (Table 3.9).

Table 3.9

Schiff's Base	Gradient($\times 10^{-3}$)	Correlation Coefficient
Chloro-	-1.5048	0.9907
Bromo-	-2.6190	0.9989
Iodo-	-15.1620	0.9843

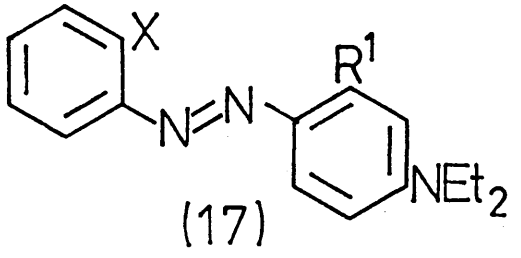
Graph 3.10



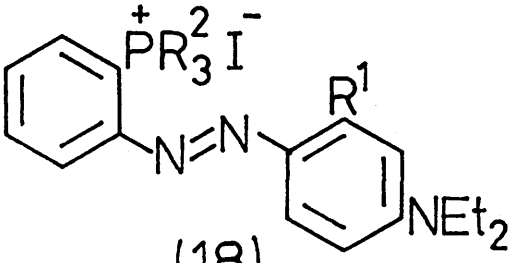
From the table, it is seen that the o-iodoaryl Schiff's base reacts approximately five times faster than the related o-bromoaryl Schiff's base, whose rate of reaction is twice as fast as the o-chloroaryl Schiff's base. Hence the order of reactivity, for the Schiff's base templates is established as I>Br>Cl.

3.5 A KINETIC STUDY OF THE NICKEL (II) CATALYSED REACTIONS OF ORTHO-HALOARYLAZO DYESTUFF TEMPLATES WITH TERTIARY PHOSPHINES

For ease of comparison with the Schiff's base study, the same reaction conditions were employed during this investigation. Detection of the ionic azodye-phosphonium salt was achieved by either conductiometric techniques (for those reactions where the wavelength separation between absorbance maxima of reactant and product was < 60 nm) or visible spectrophotometric techniques (for those > 60 nm separation). The two simple dye systems used throughout this investigation were the type II system (17; R^1=H, X=Cl, Br or I) and the type III system (17; R^1= NHCOMe, X=Cl, Br or I)



(17)



(18)

The reactions of both systems are known to be catalysed only by nickel (II) bromide to give the arylphosphonium dyestuffs (18; R^1=H or NHCOMe, R^2=Ph or Bu).

3.5.1. Dependence of Rate on Each Reactant

A similar study to that performed on the Schiff's base system was employed for both dye systems. Again similar patterns to the Schiff's base system have emerged.

(A) Dependence on the Nature of the Azo-Dye Halogen

In both dye systems, the most noticeable feature was the large range of conductivities over which the reaction of the o-iodo-substrate had to be followed. This, in turn, was much larger than for the o-bromo-dye, and, likewise, the reaction of the o-chloro-dye was followed over the shortest conductivity range. Again, this finding can be related to ionic mobilities, the smaller the ion, the larger the solvated radius and hence the lower the conductivity. It has been established, after consideration of initial slopes, that the rate of reaction with respect to the ortho-halosubstituent is again in the order of I>Br>Cl.

(B) Dependence on the Nature of the Nickel (II) Halide Catalyst

This investigation resulted in very similar findings to those observed for the Schiff's base system in that (for both the type II and III dye systems) the initial slopes of all the conductivity-time plots were approximately identical. Again the terminal conductance values differed quite remarkably, but in terms of relative rates, the pseudo-first order plots show that the identity of the halide anion in the catalyst is unimportant.

(C) Dependence on the Nature of the Phosphine

A similar study of the effects of varying the nature of the phosphine, whilst keeping the concentrations and identity of the nickel (II) catalyst and dyestuff template

constant, demonstrated that the reaction of tributylphosphine is three times faster than that of triphenylphosphine. This was true for both type II and type III azodye systems and agrees well with the related reaction of the Schiff's base templates.

(D) Dependence on the Concentration of the Phosphine

During this study the ratios of the concentrations of azodye to nickel (II) bromide catalyst were kept constant i.e. 1:0.2 moles respectively, whilst the concentration of the phosphine was changed from 1:2:3:4:5 and 10 mole equivalents respectively.

From these reactions, it was again apparent that once a minimum of phosphine is present (i.e. phosphine:dye >5:1 mole equivalents) the relative rate of reaction is constant, whereas below a mole ratio of 4:1, the initial slopes are all different. This would suggest that at concentrations above 5 mole equivalents, the phosphine has no effect on the rate of the reaction, i.e. the reaction has become zero order with respect to the phosphine.

(E) Dependence on the Concentration of the Dyestuff

During this investigation, the rates of the concentrations of phosphine to nickel (II) bromide were kept at 3:0.2 moles respectively, whilst the concentration of the azodye was varied from 0.5:1:2 and 4 mole equivalents respectively.

From conductivity - time plots, it was evident that as the concentration of the azodyestuff increases so does the relative rate of the reaction.

(F) Dependence on the Concentration of the Catalyst

In this study, the ratio of the concentrations of azodye to phosphine was held at 1:3 moles respectively, whilst the catalyst concentration ($Ni(II)Br_2$) was changed from 0.1:0.2:0.4 and 0.8 moles respectively. As with the Schiff's base system, the initial slopes of the conductivity - time plots are similar, therefore implying the same rate of reaction. However, it is only after a 24 hour period that the expected increase in rate (as the catalyst concentration is increased) is revealed.

3.5.2 Order of Reaction

The order, with respect to each reactant, was calculated in exactly the same way as for the Schiff's base system. The reactants that were chosen were the types II and III o-bromodiarylazo-dyestuffs, triphenylphosphine and nickel (II) bromide.

(A) The Order with Respect to the Phosphine

These reactions were carried out under pseudo-first order conditions and the following data (Table 3.10) were obtained from the plots of $\ln(G_\infty - Gt)$ against time (min).

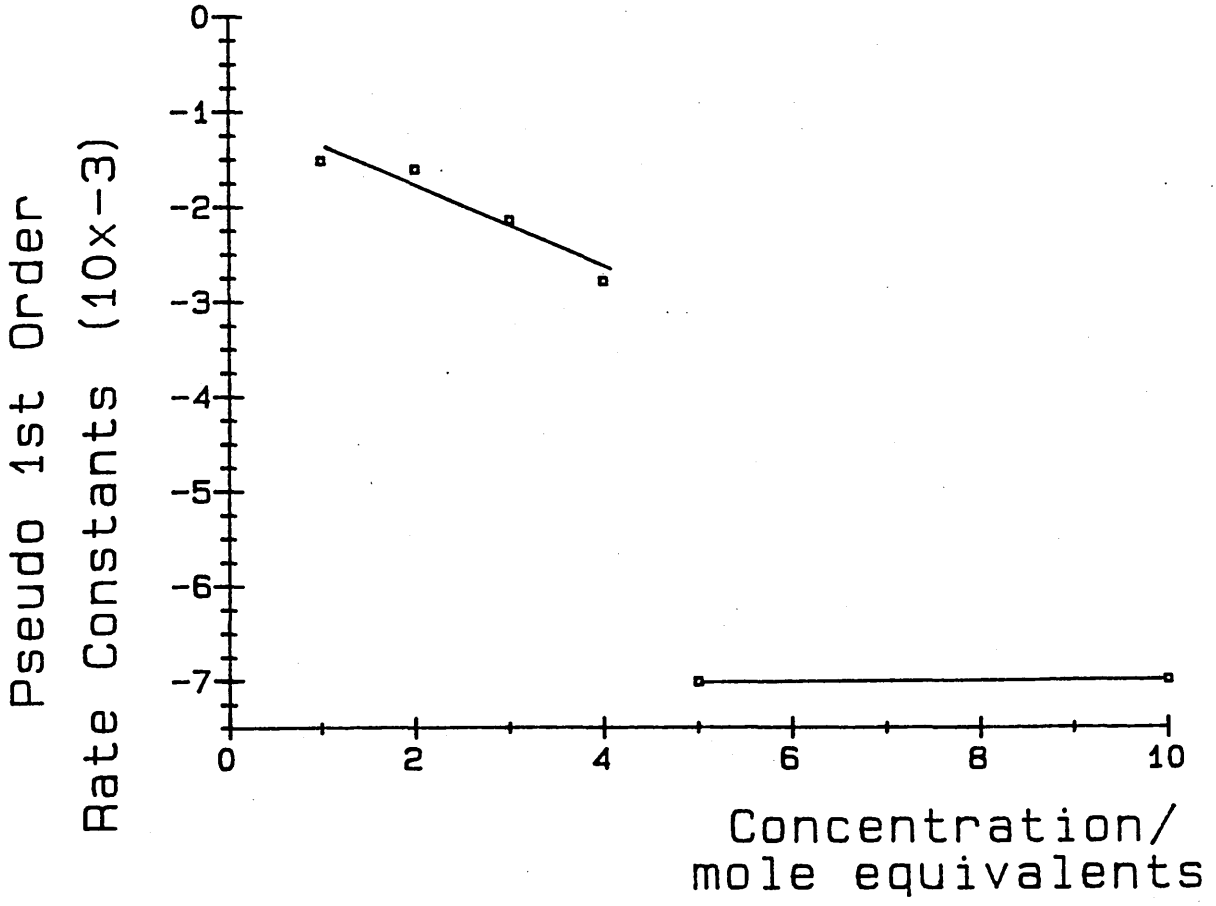
Table 3.10

Reaction of the Type III dyestuff

Mole Ratio of Phosphine:Dye (n) (1) :Catalyst (0.2)	Gradient ($x10^{-3}$)	Correlation Coefficient
n=1	-1.5236	0.9946
n=2	-1.6193	0.9936
n=3	-2.1540	0.9644
n=4	-2.7960	0.9912
n=5	-7.0128	0.9732
n=10	-6.9886	0.9888

It can be seen from the Table 3.10 and Graph 3.11 that when the phosphine:dyestuff ratio is increased above 5:1, there is no apparent change in the rate of the reaction. Yet below a rate of 4:1, there is a marked difference in the rate of each reaction. Again the same conclusion as proposed for the Schiff's base system can be made, i.e. that the order with respect to the phosphine is zero above the rate of 5:1 i.e. $[PR_3]^0$. However on the same plot, at lower concentrations of phosphine (<5:1) a first order dependence predominates.

A similar situation prevails in the reaction of the type II system, as indicated in Table 3.11 and Graph 3.12.


Pseudo 1st Order
Rate Constants (10x-3)
0
-1
-2
-3
-4
-5
-6
-7
0
2
4
6
8
10
Concentration/
mole equivalents

Graph 3.12

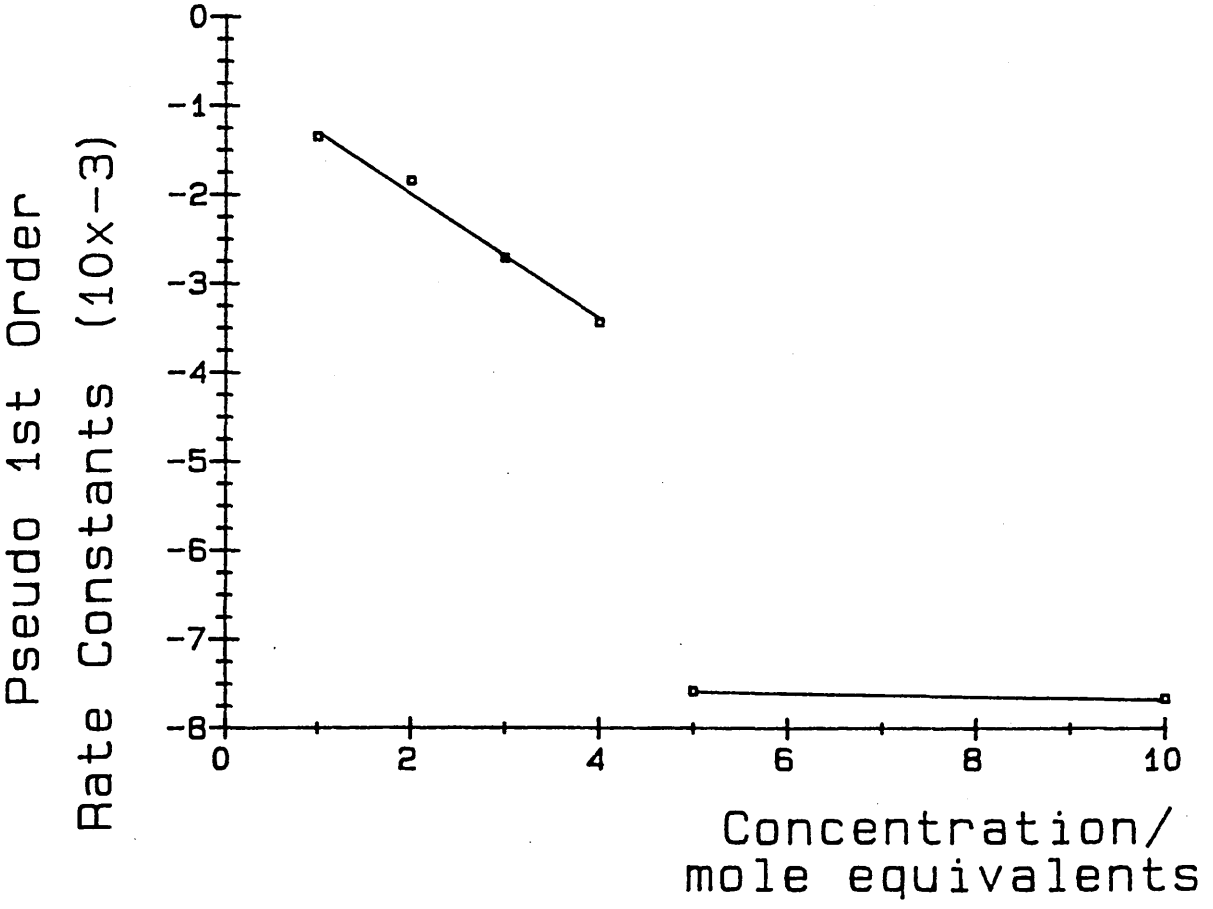

Pseudo 1st Order
Rate Constants (10x-3)
0
-1
-2
-3
-4
-5
-6
-7
-8
0
2
4
6
8
10
Concentration/
mole equivalents

Table 3.11

Reaction of Type II dyestuff

Mole Ratio of Phosphine:Dye (n) (1) :Catalyst(0.2)	Gradient ($x10^{-3}$)	Correlation Coefficient
n=1	-1.3517	0.9842
n=2	-1.8450	0.9619
n=3	-2.7131	0.9771
n=4	-3.4313	0.9889
n=5	-7.5842	0.9946
n=10	-7.6675	0.9901

(B) The Order with Respect to the Azodyestuff

The results are displayed in Tables 3.12 and 3.13 for the reactions performed under pseudo first order conditions.

Table 3.12

Reaction of Type III dyestuff

Mole Ratio of Dye:Phosphine (n) (3) :Catalyst(0.2)	Gradient ($x10^{-3}$)	Correlation Coefficient
n=0.5	-0.9409	0.9845
n=1	-1.4065	0.9958
n=2	-2.1377	0.9992
n=4	-3.4243	0.9941

Table 3.13

Reactions of Type II dyestuff

Mole Ratio of Dye:Phosphine (n) (3) :Catalyst(0.2)	Gradient ($x10^{-3}$)	Correlation Coefficient
n=0.5	-0.9015	0.9905
n=1	-1.2344	0.9573
n=2	-2.5225	0.9990
n=4	-5.3370	0.9706

* Both sets of figures were compiled from the initial slopes (up to and including 180 mins.) of the reactions carried out over a 24 hour period.

The same problem, as experienced with the Schiff's base system, occurred with the dyestuffs. Thus, for reactions conducted over a 24 hour period the rate apparently dropped as the concentration of dyestuff was increased. Consequently, the results were compiled over a smaller time scale (ca 180 minutes) and a first order dependence for both the type II - and type III - dyestuffs can be seen in the Graph 3.13.

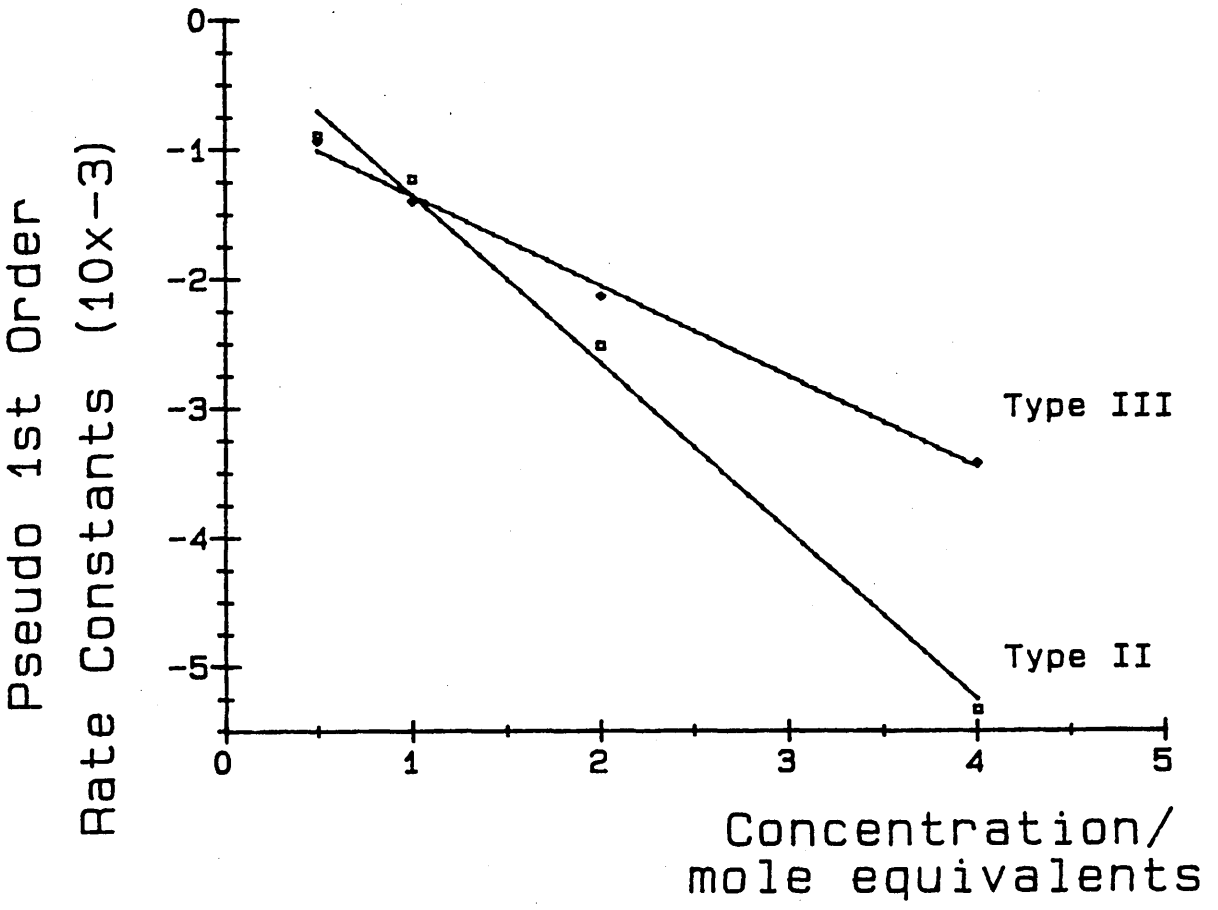
A quantitative study using the azodyestuffs (11; R^1=H or NHCOMe, X=Cl, Br or I) (1 mole):triphenylphosphine (3 moles): nickel (II) bromide (0.2 moles) confirmed the qualitative observation that the order of reactivity is I>Br>Cl. Again (cf Schiff's base system) it has been possible to obtain straight line plots for the first six data points of each of the reactions of the chloro-, bromo- and iodo- arylazodyestuffs by plotting $\ln(G_\infty - Gt)$ against time. The results are illustrated in Table 3.14.

Table 3.14

Table of $\ln(G_\infty - Gt)$ values for type II and III azodyestuffs

	TYPE II			TYPE III		
T/min	Chloro-	Bromo-	Iodo-	Chloro	Bromo-	Iodo-
0	3.67	5.02	5.11	3.05	5.12	5.34
30	3.53	5.00	2.22	3.03	5.00	5.18
60	3.37	4.67	1.53	3.00	4.97	5.04
90	3.20	4.16	-0.63	2.99	4.92	4.72
120	3.07	3.59	-2.41	2.96	4.89	4.50
150	2.91	3.06	-	2.94	4.82	4.01

Graph 3.15

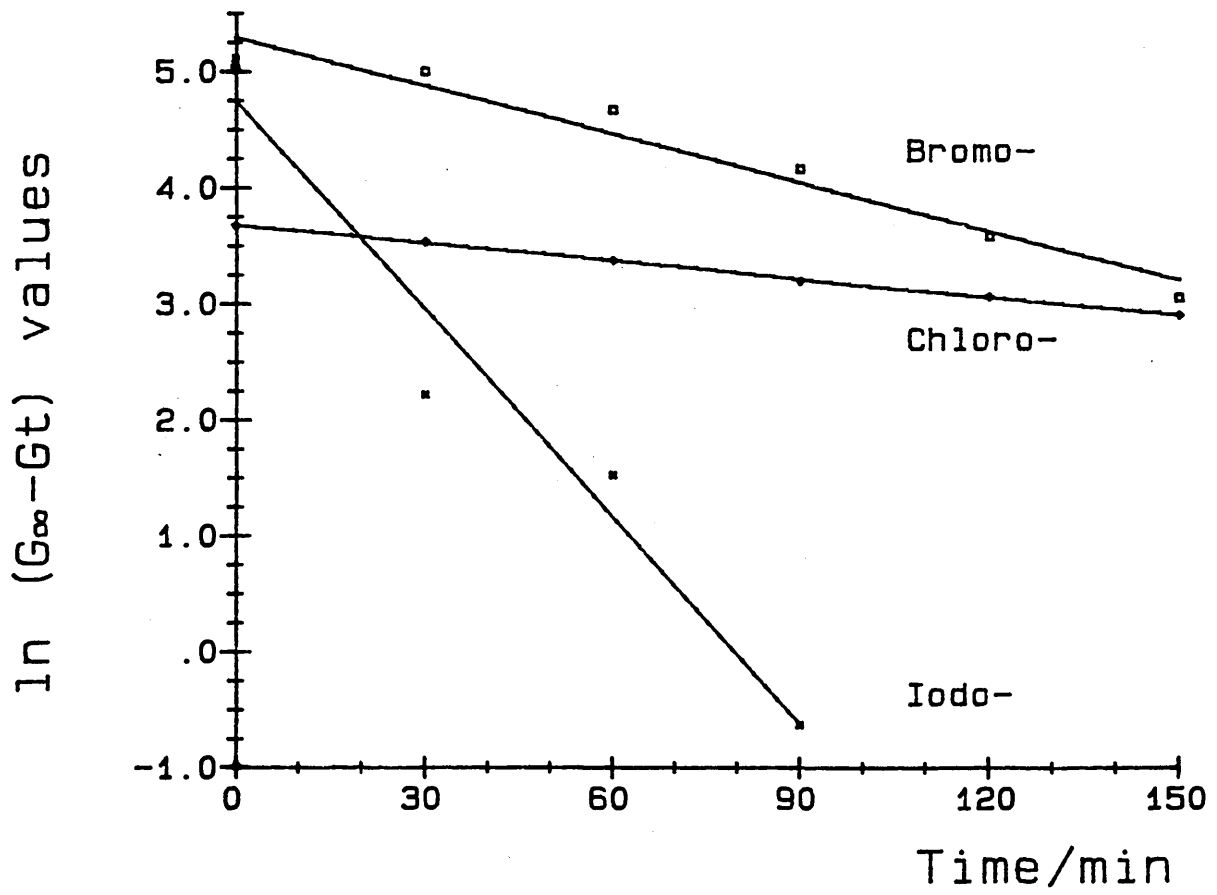


A comparison of the gradients of the straight line plots (Graphs 3.14 and 3.15) reveals the relative rates of reaction for both the type II and type III arylazodyestuffs.

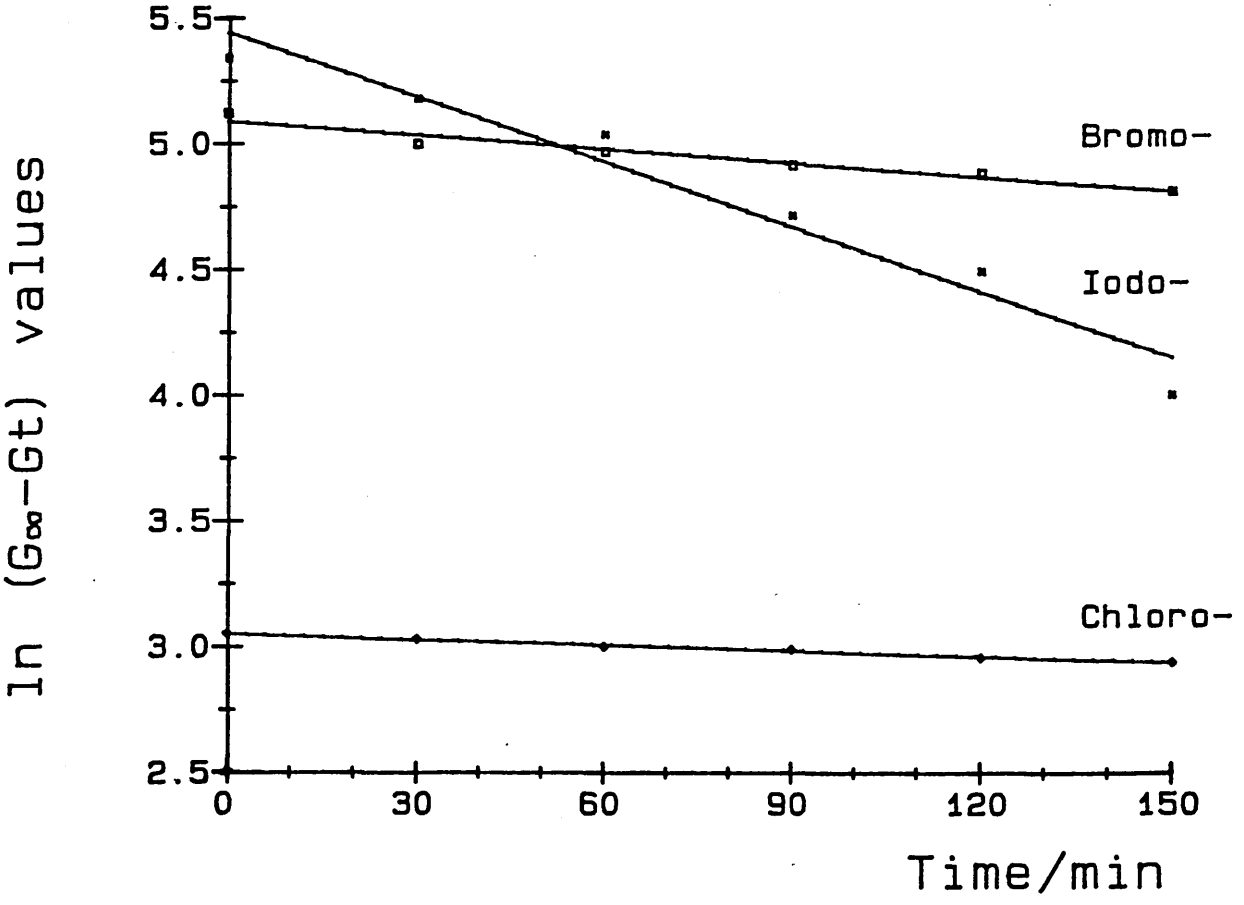
Table 3.15

Dyestuff	Gradient($x10^{-3}$)	Corrrelation Coefficient
Type II Chloro-	-5.0952	0.9995
Bromo-	-13.848	0.9728
Iodo-	-59.633	0.9876
Type III Chloro-	-0.7333	0.9953
Bromo-	-1.7905	0.9748
Iodo-	-8.5810	0.9774

From the above table, it is seen that the o-iodoarylazo dyestuffs (both type II and III) react approximately


5.0
4.0
3.0
2.0
1.0
.0
-1.0
0
30
60
90
120
150
ln (G∞-Gt) values
Time/min
Bromo-
Chloro-
Iodo-

Graph 3.15

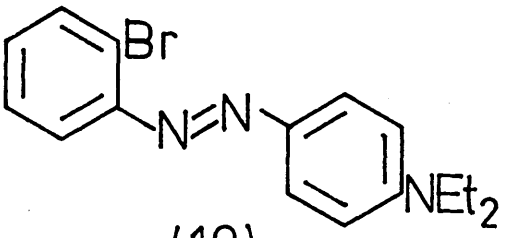

5.5
5.0
4.5
4.0
3.5
3.0
2.5
0
30
60
90
120
150
ln (G∞-Gt) values
Time/min
Bromo-
Iodo-
Chloro-

five times faster than the related o-bromoarylazo dyestuffs, whose rates of reaction are two and a half times as fast as for the o-chloroarylazo dyestuffs. Hence the order of the reactivity, for the type II and III dyestuff templates follows the series I>Br>Cl. These results compare well with the earlier Schiff's base study and it seems apparent from the results that the iodo-systems are far more reactive than either the bromo- or chloro-systems.

A direct comparison of relative rates between both the Schiff's base and azodyestuff systems reveals that for the nickel (II) - catalysed template reactions, the type II systems react faster than the type III system. On closer inspection (c.f. Tables 3.9 and 3.15) it can be established that the magnitude of relative rates is approximately in the order of:-

Type II dye	:	Schiff's base	:	Type III dye
7	:	2	:	1

Perhaps it is unrealistic to compare the Schiff's base results with those of the azodyestuffs because of (a) the difference between imino and azo linkages and, (b) the difference in the identity of the para-substituent (OMe vs NEt_2). Hence, a comparison of the slopes of the azodyestuff (19) against the Schiff's base (20) shows that the type II azodyestuff is undergoing the reaction only two and a half times faster than the related Schiff's base (20) as opposed to three and a half times faster, when the para-substituent is OMe.



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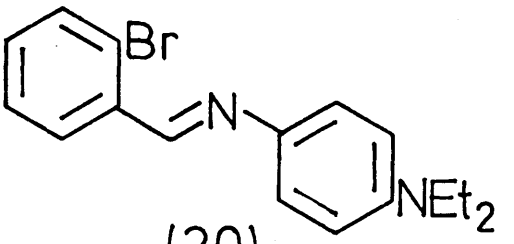


(20)

(C) The Order with Respect to the Catalyst

The results of this study are shown in the Tables 3.16 and 3.17 below.

Table 3.16 Reactions of Type III dyestuff

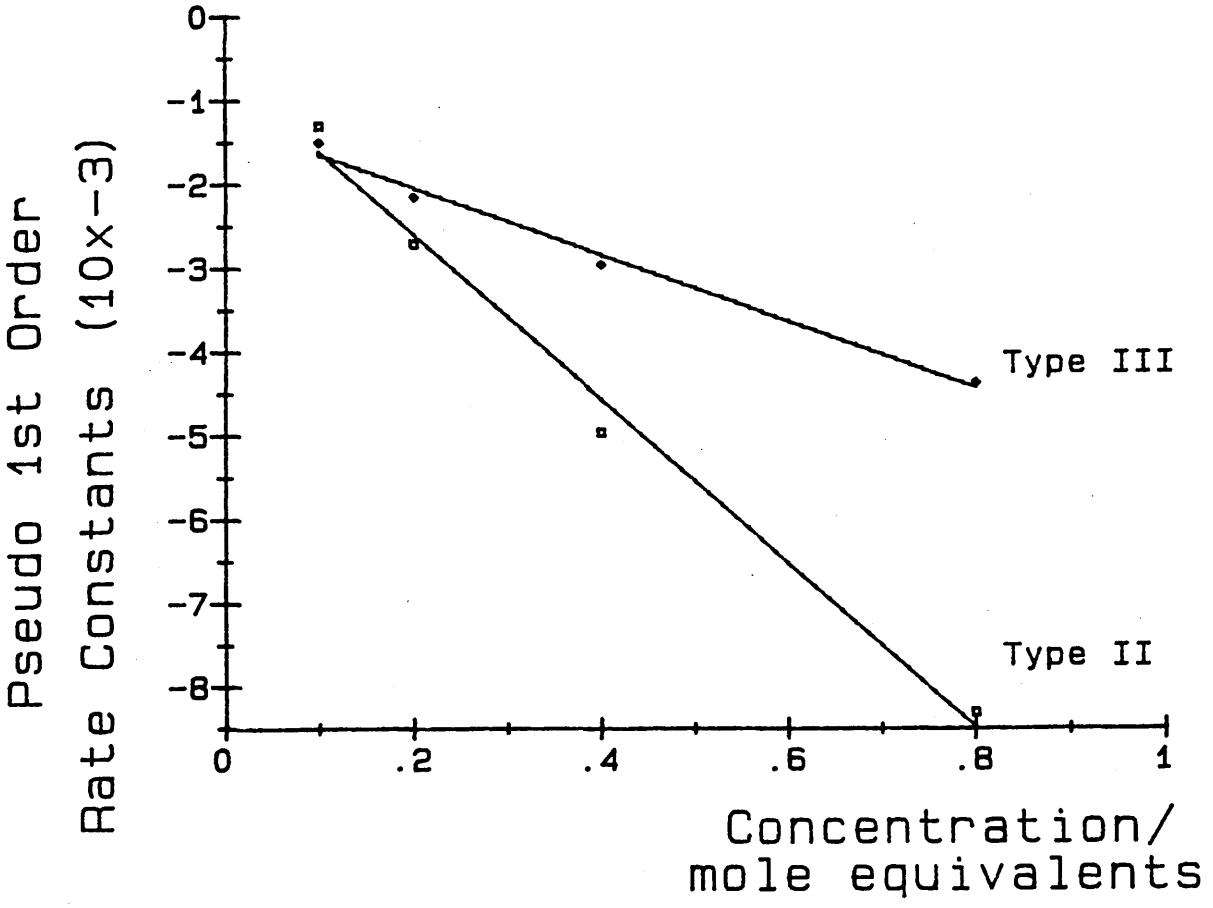
Mole Ratio of Catalyst:Dye (n) (1) :Phosphine(3)	Gradient ($x10^{-3}$)	Correlation Coefficient
n=0.1	-1.5053	0.9691
n=0.2	-2.1540	0.9644
n=0.4	-2.9563	0.9725
n=0.8	-4.3621	0.9932

Table 3.17 Reactions of Type II dyestuff

Mole Ratio of Catalyst:Dye (n) (1) :Phosphine(3)	Gradient ($x10^{-3}$)	Correlation Coefficient
n=0.1	-1.3109	0.9816
n=0.2	-2.7131	0.9771
n=0.4	-4.9574	0.9950
n=0.8	-8.3066	0.9773

From the results, it can be demonstrated (for both the type II and III arylazodyestuffs) that as the concentration of catalyst increases, then the rate of the reaction

Graph 3.16



(i.e. gradient) increases. A plot of these reaction gradients against the catalyst concentration (Graph 3.16) reveals a first order dependence with respect to the catalyst in both dye systems.

3.6 ADDITIONAL INVESTIGATIONS

Several additional investigations were undertaken which supplemented the kinetic studies and which shed further light on the possible mechanism of these reactions. They included reactions (a) using preformed complexes, (b) radical scavengers, and (c) reactions conducted in the dark.

3.6.1 Reactions with Preformed Complexes

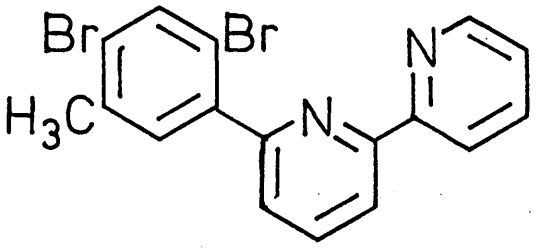
The main problem with using the preformed nickel (II) complexes (21; X=Cl, Br or I) was their initial insolubility in boiling ethanol. Therefore no reliable conductiometric measurements could be obtained for these types of reaction. The preformed copper (I) complexes (22; X=Cl or Br) failed to react with any o-haloaryl templates [except the halide (23) which formed a copper -bipyridyl complex with (22)]. Similarly, the silver-phosphine complex[12](24) failed to react with any template-substrates to produce phosphonium salts.

$(Ph_3P)_2NiX_2$

(21)

$[(Ph_3P)CuXiX]_4$

(22)



(23)

$(Ph_3P)_3AgCl$

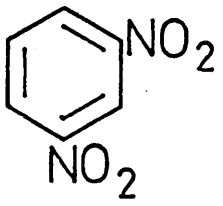
(24)

Overall yield studies showed that reactions involving the preformed nickel (II) complex (19) are quantitative after only 8 hours (when used in a 1:1 ratio with the substrate) as opposed to 24 hours when a ratio of triphenylphosphine:nickel (II) bromide (3:0.2 moles) is employed. This seems to imply that the preformed complex 'speeds up' the rate of reaction. This result is most probably attributed to a concentration effect.

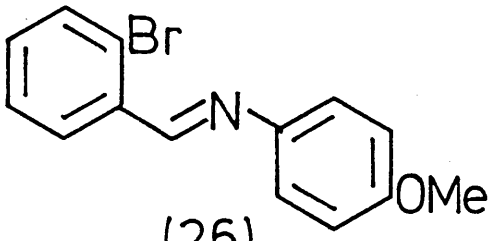
3.6.2 Reactions Involving Radical Scavengers

A recognised radical scavenger, meta-dinitrobenzene (25) was employed during this investigation. It was used in the reactions of the Schiff's base (26) and the azodyestuffs (19) and (27) at a concentration equal to that of the catalyst. In every case, the presence of the radical scavenger failed to either (a) alter the course or (b) slow down the rate of the substitution reaction.

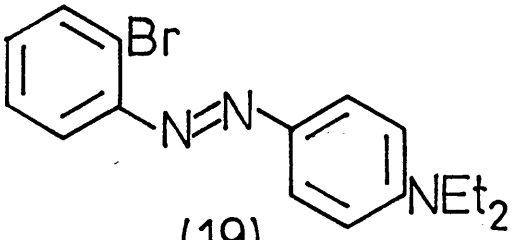
A similar study of the reactions of each of the substrates (19, 26 and 27) in the dark also failed to prevent formation of arylphosphonium salts. Thus, the



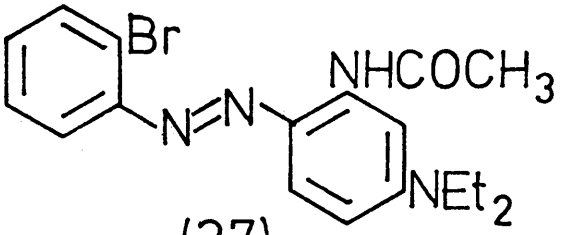
(25)



(26)



(19)



(27)

last two studies have shown that it is likely that radicals are not involved in the mechanism of these substitution reactions.

3.7 CONCLUSIONS AND EVALUATION OF THE MECHANISTIC SCHEME

The mechanistically - significant data obtained in the above rate study may be summarized as follows:-

(a) The phosphonium salt formation reactions show a first order dependence on the concentration of each reactant, i.e.

rate α [template substrate] [phosphine] [catalyst]

(b) For both Schiff's base and azodye templates, the order of reactivity of the ortho-halogen replaced is I>Br>Cl.

(c) In the Schiff's base system, electron-donating substituents present in the aryl ring attached to the imino-nitrogen increase the rate of the reaction. The opposite is true for electron-withdrawing substituents.

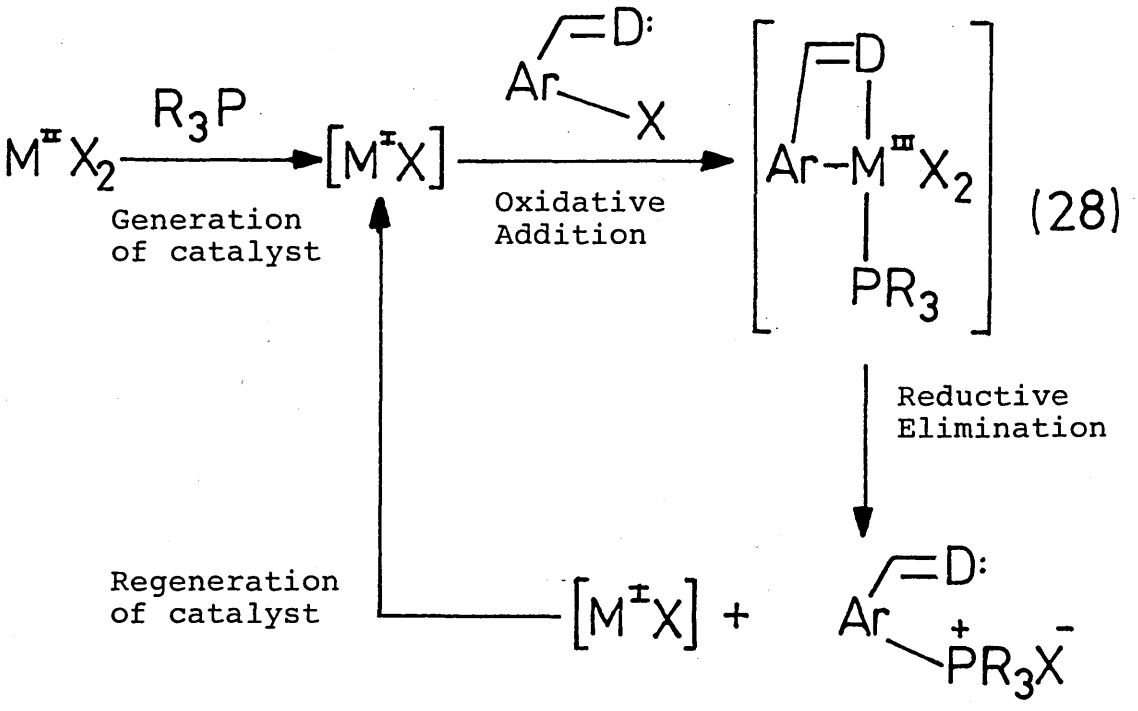
(d) The nature of the halogen present in the nickel (II) halide catalyst is not significant.

(e) Radical processes do not appear to be involved in these reactions

(f) Increasing steric crowding in the simple dyestuff templates reduces the rate of the substitution reaction.

(g) The more nucleophilic the phosphine, the faster the rate of the reaction.

All of the above observations may be accounted for in the mechanistic scheme which has been previously proposed (Scheme 1):-



(Scheme 1)

It is likely that these template reactions involve electron-transfer catalysis[13] in which the metal is initially reduced to a lower oxidation state, e.g. $Ni^{II} \longrightarrow Ni^{I}$ (the active catalytic species), which then undergoes a co-ordination template assisted oxidative insertion into the carbon-halogen bond, followed by formation of the phosphorus-carbon bond in a reductive-elimination of the product, with regeneration of the catalyst.

Thus dependence of the rate on the catalyst and the order of halogen displacements are consistent with the involvement of an oxidative insertion of a metal-phosphine complex into the carbon-halogen bond at a crucial stage of the reaction. There are many examples

in the literature in which a similar rate dependence is observed for reactions involving an oxidative insertion step[14-16]. From studies of the nature of the donor site in the template reported by Allen et al[1] and also in this thesis, it is clear that the donor centre must involve ortho-donor/π -acceptor character; facilitating coordination to the nickel (or copper) atom in the key intermediate e.g. (28).

3.8 EXPERIMENTAL

The following compounds have been prepared as previously described:- N-(2-chlorobenzylidene)-4-methoxyaniline (5; X=Cl)[17], N-(2-bromobenzylidene)-4-methoxyaniline (9)[1], 4-Methoxy-N-(2-triphenylphosphoniobenzylidene)aniline bromide (10; R=Ph)[1], 4-Methoxy-N-(2-tributylphosphoniobenzylidene)aniline bromide (10; R=Bu)[1], Bis(triphenylphosphine)nickel (II) halide (21; X=Cl, Br, I)[18], Bis(tributylphosphine)nickel (II) halide (15; R=Bu; X=Cl or Br)[19], Tetrakis[bromotriphenylphosphine copper (II)] (22; X=Br)[20], Tetrakis[chlorotriphenylphosphine copper (I)] (22; X=Cl)[20] and 'Super Dry' Ethanol[21]. The following compounds appear to be new.

3.8.1 Preparation of Schiff's Bases

The Schiff's bases N-(2-fluorobenzylidene)-4-methoxyaniline (5; X=F) and N-(2-iodobenzylidene)-4-methoxyaniline (5; X=I) were prepared by heating together equimolar quantities of the appropriately ortho-substituted benzaldehyde and para-anisidine in boiling ethanol under a nitrogen atmosphere for 1-2 hours. The solids crystallized on cooling. After filtration they were purified by recrystallisation giving the products:-

N-(2-Fluorobenzylidene)-4-methoxyaniline (5, X=F) This was isolated as a pale green solid (56%) m.p. 47°C (From cyclohexane) (Found C 79.01, H 5.61, N 6.60: $C_{14}H_{12}N_1F_1$ requires C 78.87, H 5.63, N 6.57%) δ^1H($CDCl_3$) 8.7(s,1H), 8.1-6.9(m,8ArH), 3.85(s,3H)ppm.

N-(2-Iodobenzylidene)-4-methoxyaniline (5, X=I) This was isolated as lime-green crystals (66%) m.p. 63°C (From EtOH) (Found C 52.10, H 3.73, N 4.40: $C_{14}H_{12}N_1I_1$ requires C 52.34, H 3.74, N 4.36%) $\delta^1H(CDCl_3)$ 8.6(s,1H), 8.1-6.9(m,8ArH), 3.9(s,3H)ppm.

The Schiff's bases derived from o-bromobenzaldehyde and different para-substituted aniline derivatives were prepared under exactly the same conditions as reported earlier in Chapter 2, they included:-

N-(2-Bromobenzylidene)-4-methylaniline (6, R=Me) This was isolated as beige-coloured crystals (49%) m.p. 38°C (From EtOH) (Found C 61.28, H 4.38, N 4.98: $C_{14}H_{12}Br_1N_1$ requires C 61.33, H 4.41, N 5.10%) $\delta^1H(CDCl_3)$ 8.75(s,1H) 8.2-7.0 (m,8ArH) 2.25(s,3H)ppm. m/e 274 [$M^+(^{81}Br)$].

N-(2-Bromobenzylidene)aniline (6, R=H) This was obtained as a brown liquid (63%) b.p. 120°C at 0.5 mmHg. (Found C 60.10, H 3.83, N 5.45: $C_{13}H_{10}Br_1N_1$ requires C 60.00, H 3.85, N 5.38%) $\delta^1H(CDCl_3)$ 8.75(s,1H) 8.2-6.9(m,9ArH)ppm.

N-(2-Bromobenzylidene)-4-bromoaniline (6, R=Br) This was isolated as a light green solid (94%) m.p. 78°C (From EtOH) (Found C 46.17, H 2.58, N 3.98: $C_{13}H_9Br_1N_1$ requires C 46.05, H 2.67, N 4.13%) $\delta^1H(CDCl_3)$ 8.7(s,1H) 8.2-7.0(m,8ArH)ppm. m/e 339[$M^+(^{81}Br)$].

N-(2-Bromobenzylidene)-4-nitroaniline (6, R=NO_2) This was collected as pale green crystals (80%) m.p. 125°C (From EtOH) (Found C 51.69, H 3.40, N 9.48: $C_{13}H_9Br_1N_2O_2$ C 51.17, H 2.97, N 9.18%) $\delta^1H(CDCl_3)$ 8.75(s,1H) 8.3-7.15 (m,8ArH)ppm. m/e 304 [$M^+(^{81}Br)$].

N-(2-Bromobenzylidene)-4-phenylaminoaniline (6, R=NHPh) This was isolated as bright green crystals (99%) m.p. 78°C (From EtOH) (Found C 65.01, H 4.27, N 7.70: $C_{19}H_{15}Br_1N_2$ requires C 64.97, H 4.30, N 7.97%) $\delta^1H(CDCl_3)$ 8.7(s,1H) 8.2-6.85(m,13ArH) 5.8(s, very broad, 1H)ppm. m/e 351 $[M^+(^{81}Br)]$.

N-(2-Bromobenzylidene)-4-hydroxyaniline (6, R=OH) This was obtained as a pale green solid (21%) m.p. 151°C (From EtOH) (Found C 56.58, H 3.61, N 4.92: $C_{13}H_{10}Br_1N_1O_1$ requires C 56.54, H 3.65, N 5.07%) $\delta^1H(CDCl_3)$ 8.75(s,1H), 8.1-6.85 (m,8ArH), 5.15(s,1H)ppm. m/e 276 $[M^+(^{81}Br)]$.

N-(2-Bromobenzylidene)-4-diethylaminoaniline (6, R=NEt_2) This was isolated as bright yellow crystals (79%) m.p. 72°C (From EtOH) (Found C 61.48, H 5.83, N 8.23: $C_{17}H_{19}Br_1N_2$ requires C 61.64, H 5.78, N 8.45%) $\delta^1H(CDCl_3)$ 8.7(s,1H) 8.2-7.2(m,4ArH) 7.3-6.6(simple $[AX]_2$ system, 4ArH) 3.35 (q,4H) 1.2(t,6H)ppm. m/e 331 $[M^+(^{81}Br)]$.

N-(2-Bromobenzylidene)-4-cyanoaniline (6, R=CN) This was obtained as cream coloured crystals (54%) m.p. 118°C (From EtOH) (Found C 58.91, H 3.25, N 9.90: $C_{14}H_9Br_1N_2$ requires C 58.97, H 3.18, N 9.82%) $\delta^1H(CDCl_3)$ 8.8(s,1H) 8.3-6.6(m,8ArH)ppm

N-(2-Bromobenzylidene)-4-carboexthoxyaniline (6, R=CO_2Et) This was isolated as pale yellow crystals (62%) m.p. 70-72°C (From EtOH) (Found C58.05, H 4.36, N 4.40: $C_{16}H_{14}Br_1N_1O_2$ requires C 57.85, H 4.25, N 4.22%) $\delta^1H(CDCl_3)$ 8.7(s,1H) 8.1-7.2(m,8ArH) 4.2(q,2H) 1.2(t,3H)ppm.

3.8.2 Preparation of Azodyestuffs

To a flask containing concentrated hydrochloric acid (12cm^3) and an equal amount of water was added the o-haloaniline substituent (0.03 moles) which was dissolved by heating. The reaction mixture was then cooled in an ice bath to below 5°C, whereupon a solution of sodium nitrite (0.033 moles ca 10% w/v) was added dropwise over a period of 5 minutes. Since the diazotisation reaction is exothermic, the following conditions must be observed during the procedure:-

a) Acidity to congo-red paper

b) A positive reaction to starch-iodide paper

c) A temperature <10°C

After continuous stirring for 15 minutes in the presence of excess nitrous acid, sulphamic acid was added to the solution until a negative test on starch iodide paper was observed. The diazonium salt solution was filtered into a solution of the diethylaniline component (0.03 moles) dissolved in water (22 cm^3) and concentrated hydrochloric acid (22 cm^3) at 10°C. The resulting mixture was then stirred for a further 10 minutes. Sodium acetate crystals were added until the reaction mixture was no longer acid to congo-red paper. The mixture was left standing overnight. The resulting solid dye was filtered, washed with water, and left to dry in air. The crude azodye was then recrystallised from ethanol. The following azodyestuffs were prepared:

1-(2-Chlorophenylazo)-4-N,N-diethylaminobenzene (7, X=Cl) This was isolated as red crystals (52%) m.p. 60°C (From EtOH) (Found C 66.12, H 6.41, N 14.56: $C_{16}H_{18}Cl_1N_3$ requires C 66.77, H 6.30, N 14.60%) δ ^{1}H($CDCl_3$) 7.9-6.8 ($[AX]_2$ system, 4ArH), 7.75-7.2(m,4ArH), 3.5(q,4H) 1.2(t,6H)ppm.

1-(2-Bromophenylazo)-4-N,N-diethylaminobenzene (7, X=Br) This was obtained as red crystals (53%) m.p. 61% (From EtOH) (Found C 57.87, H 5.53, 12.62: $C_{16}H_{18}Br_1N_3$ requires C 57.84, H 5.46, N 12.64%) δ ^{1}H($CDCl_3$) 7.9-6.7($[AX]_2$ system, 4ArH), 7.6-7.1(m,4ArH), 3.5(q,4H), 1.25(t,6H)ppm.

1-(2-Iodophenylazo)-4-N,N-diethylaminobenzene (7, X=I) This was isolated as red crystals (41%)m.p. 71°C (From EtOH) (Found C 50.21, H 4.72, N 10.97: $C_{16}H_{18}I_1N_3$ requires C 50.67, H 4.78, N 11.08%) δ ^{1}H($CDCl_3$) 8.0-6.9($[AX]_2$ system, 4ArH), 7.8-7.2(m,4ArH), 3.5(q,4H), 1.25(t,6H)ppm.

1-(2-Chlorophenylazo)-2-acetylamino-4-N,N-diethylaminobenzene (8, X=Cl) This was isolated as red crystals (42%) m.p. 99°C (From EtOH) (Found C 62.42, H 6.37, N 16.34: $C_{18}H_{21}Cl_1N_4O_1$ requires C 62.69, H 6.13, N 16.24%) δ ^{1}H($CDCl_3$) 8.3(s,1ArH), 7.8(d,2ArH), 7.4(m,4ArH), 6.5(d,1H), 3.5(q,4H), 2.3(s,3H), 1.3(t,3H)ppm.

1-(2-Bromophenylazo)-2-acetylamino-4-N,N-diethylaminobenzene (8, X=Br) This was isolated as red crystals (75%) m.p. 101°C (From EtOH) (Found C 55.13, H 5.31, N 14.08: $C_{18}H_{21}Br_1N_4O_1$ requires C 55.53, H 5.43, N 14.39%) δ ^{1}H($CDCl_3$) 8.3(s,1ArH), 7.75(d,2ArH), 7.3(m,4ArH), 6.5(d,1H), 3.5(q,4H), 2.3(s,3H), 1.25(t,3H)ppm.

1-(2-Iodophenylazo)-2-acetylamino-4-N,N-diethylaminobenzene (8, X=I) This was obtained as red crystals (47%) m.p. 111°C (From EtOH) (Found C 49.88, H 4.72, N 12.90 $C_{18}H_{21}I_1N_4O_1$ requires C 49.55, H 4.85, N 12.84%) δ 1H($CDCl_3$) 8.35(s,1ArH), 7.8(d,2ArH), 7.4(m,4ArH), 6.5(d,1H), 3.55 (q,4H), 2.3(s,3H), 1.2(t,3H)ppm.

3.8.3 Preparation of Phosphonium Salts

The template (10^{-3}mole), tertiary phosphine ($3x10^{-3}$ moles) and nickel (II) bromide ($2x10^{-4}$ moles) were heated together under reflux in ethanol (10 cm^3) in a nitrogen atmosphere for 5-8 hours. The reaction mixture was then poured into water (50cm^3) containing KBr or KI (0.5g), and extracted with ether (2x20 cm^3) in order to remove any non-ionic impurities. The aqueous layer was then extracted with chloroform (3x10 cm^3) and discarded. The chloroform layer was dried ($MgSO_4$) and evaporated. The oily residue was then triturated several times with sodium - dried ether until it solidified. After filtration, the majority of salts were recrystallised using a chloroform/ethylacetate mixture. All the butylphosphonium salts became hygroscopic on contact with the atmosphere and therefore no microanalytical data has been obtained on these salts. During the kinetic study the following salts have been characterised:

4-Methyl-N-(2-triphenylphosphoniobenzylidene)aniline iodide (16, R=Me) This was isolated as yellow crystals (42%) m.p. >300°C (From $CHCl_3$/EtOAc) (Found C 68.41, H 4.77,

N 3.49, $C_{37}H_{30}I_1N_2P_1$ Requires C 67.27, H 4.57, N 4.24%) $\delta^{31}P(CDCl_3)$ 25.94 ppm. $\delta^1H(CDCl_3)$, 8.5(s,1H), 7.65(m,19ArH), 6.85-5.95($[AX]_2$ system, 4ArH), 2.15(s,3H)ppm.

N-(2-triphenylphosphoniobenzylidene)aniline iodide (16, R=H) This was obtained as yellow crystals (35%) m.p. >300°C (From $CHCl_3$/ether) (Found C 63.63, H 4.35, N 2.18: $C_{35}H_{34}I_1N_2P_1 . H_2O$ requires C 63.37, H 4.60, N 2.39%) $\delta^{31}P(CDCl_3)$ 26.05 ppm. $\delta^1H(CDCl_3)$ 8.6(s,1H), 8.1-7.1 (m,24ArH)ppm.

4-Bromo-N-(2-triphenylphosphoniobenzylidene)aniline iodide (16, R=Br) This was collected as light brown coloured crystals (56%) decomp. 200-202°C (From $CHCl_3$/ether) (Found C 57.23, H 3.85, 2.21: $C_{31}H_{24}Br_1I_1N_1P_1$ requires C 57.43, H 3.73, N 2.16%) $\delta^{31}P(CDCl_3)$ 26.17ppm. $\delta^1H(CDCl_3)$ 8.8(s,1H) 8.2-7.3(m,19ArH) 7.15-6.00($[AX]_2$ system, 4ArH)ppm.

4-Phenylamino-N-(2-triphenylphosphoniobenzylidene)aniline iodide (16, R=NHPh) This was isolated as bright orange crystals (78%) decomp. 106°C (From $CHCl_3$/ether) (Found C 67.63, H 4.82, N 4.12: $C_{37}H_{30}I_1N_2P_1$ requires C 67.27, H 4.57, N 4.24%) $\delta^{31}P(CDCl_3)$ 25.72ppm. $\delta^1H(CDCl_3)$ 8.5(s,1H) 8.2-7.3(m,24ArH), 6.85-6.00($[AX]_2$ system, 4ArH) 5.7(s,1H)ppm.

4-Hydroxy-N-(2-triphenylphosphoniobenzylidene)aniline iodide (16, R=OH) This was isolated as a yellow solid (21%) m.p. >300°C (From $CHCl_3$/ether) (Found C 61.29, H 4.13, N 2.32: $C_{31}H_{25}I_1N_1O_1P_1 . H_2O$ requires C 61.69, H 4.47, N 2.32%) $\delta^{31}P(TFA/D_2O)$ 26.56ppm $\delta^1H(TFA,D_2O)$ 8.7(s,1H) 8.1-7.2(m,19ArH) 7.0-6.1($[AX]_2$ system, 4ArH) 5.2(s,1H)ppm.

4-Diethylamino-N-(2-triphenylphosphoniobenzylidene)aniline iodide (16, R=NEt_2) This was obtained as orange crystals (65%) m.p. 255°C (From $CHCl_3$/EtOAc) (Found C 64.52, H 5.31, N 4.21: $C_{35}H_{34}I_1N_2P_1$. H_2O requires C 63.83, H 5.47, N 4.26%) $\delta^{31}P(CDCl_3)$ 25.68ppm. $\delta^1H(CDCl_3)$ 8.5(s,1H) 8.1-7.1(m,19ArH) 7.3-6.2(m$[AX]_2$ system, 4ArH), 3.3(q,4H), 1.2(t,6H)ppm.

4-Carboethoxy-N-(2-triphenylphosphoniobenzylidene)aniline iodide (16, R=CO_2Et) This was isolated as light green crystals (35%) decomp. 120°C (From $CHCl_3$/EtOAc) (Found C 61.57, H 4.50, N 1.77: $C_{33}H_{29}I_1N_1O_1P_1$. H_2O requires C 61.21, H 4.79, N 1.55%) $\delta^{31}P(CDCl_3)$ 26.07ppm. $\delta^1H(CDCl_3)$ 8.5(s,1H) 8.1-7.2(m,23ArH), 4.3(q,2H), 1.3(t,3H)ppm.

All the azodyestuff salts prepared during this kinetic study were isolated and characterised with the iodide counter-anion as standard. This was achieved by adding potassium iodide crystals in the salt-isolation procedure.

4-(2-Triphenylphosphoniophenylazo)-N,N-diethylaniline iodide (12, R^1=H, R^2=Ph) This was obtained as red crystals (83%) m.p. 220°C (From $CHCl_3$/EtOAc) (Found C 62.78, H 5.13, N 6.18: $C_{34}H_{33}I_1N_3P_1$. H_2O requires C 61.91, H 5.31, N 6.37%). $\delta^{31}P(CDCl_3)$ 23.74ppm. $\delta^1H(CDCl_3)$ 8.2-7.4 (m,19ArH), 6.95-6.4($[AX]_2$ system, 4H), 3.4(q,4H), 1.2 (t,6H)ppm.

4-(2-Tributylphosphoniophenylazo)-N,N-diethylaniline iodide (12, R^1=H, R^2=Bu) This was obtained as a hygroscopic red solid (43%) $\delta^{31}P(CDCl_3)$ 31.63 ppm. $\delta^1H(CDCl_3)$ 8.5(s,4ArH), 7.1-6.6($[AX]_2$ system, 4ArH), 3.4(q,4H), 2.85(m,6H), 1.5-0.8 (m,27H) ppm.

2-Acetylamino-4-(2-triphenylphosphoniophenylazo)-N,N-diethylaniline iodide (12; R^1=$NHCOCH_3$, R^2=Ph) This was isolated as purple crystals (87%) m.p. 235°C (From $CHCl_3$/EtOAc) (Found C 61.93, H 5.29, N 7.44: $C_{36}H_{36}I_1N_4O_1P_1$ requires C 61.89, H 5.16, N 8.02%) $\delta^{31}P(CDCl_3)$ 23.43 ppm. $\delta^1H(CDCl$) 8.3-7.4(m,23ArH), 6.1(d,1H), 3.4(q,4H), 2.3(S,3H), 1.2(t,6H)ppm.

2-Acetylamino-4-(2-tributylphosphoniophenylazo)-N,N-diethylaniline iodide (12; R^1=$NHCOCH_3$, R^2=Bu) This was isolated as a hygroscopic purple solid (42%). $\delta^{31}P(CDCl_3)$ 31.05 ppm. $\delta^1H(CDCl_3)$, 8.1-7.5(m,7ArH), 6.0(d,1H), 3.4(q,4H), 2.9(m,6H), 2.35(s,3H) 1.4-0.8(m,27H)ppm.

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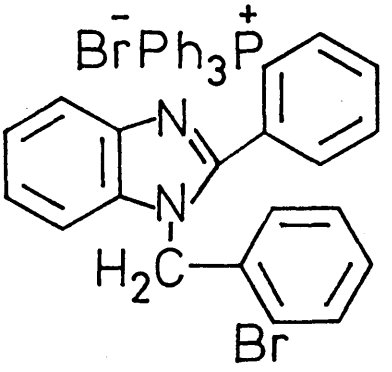
CHAPTER 4: CRYSTAL STRUCTURES OF TWO TETRAARYL-PHOSPHONIUM SALTS ISOLATED FROM TEMPLATE ASSISTED REACTIONS

4.1 INTRODUCTION

The formation of arylphosphonium salts from the reactions of tertiary phosphines with aryl halides are normally conducted at elevated temperatures (150-200°C), usually in the absence of a solvent, but always in the presence of a transition metal salt catalyst[1-4], e.g., nickel (II) bromide or cobalt (II) bromide. The introduction of a suitable donor atom (e.g. nitrogen or oxygen) ortho to the halogen leaving group allows these reactions to proceed under mild conditions (refluxing ethanol) involving the operation of a "kinetic template effect" to produce the arylphosphonium salt. In this section, the crystal structures of two arylphosphonium salts isolated from template assisted reactions are discussed.

The two arylphosphonium salts were both prepared by prolonged heating of the appropriate template (1 mol equiv.) with triphenylphosphine (3 mol equiv.) under reflux in ethanol, in the presence of nickel (II) bromide. The first salt studied triphenyl-2-(1-(2-bromobenzyl)-2-benzimidazolyl)phenylphosphonium bromide (1) was prepared from the benzimidazole (2) (Chapter 2, Section 2.3.1), and the second structure, 3-(2-triphenylphosphonio-4-bromo-5-methylphenyl)2,2′-bipyridyl bromide (3) from the aryl halide (4), donated by I.C.I., Organics Division, Manchester.



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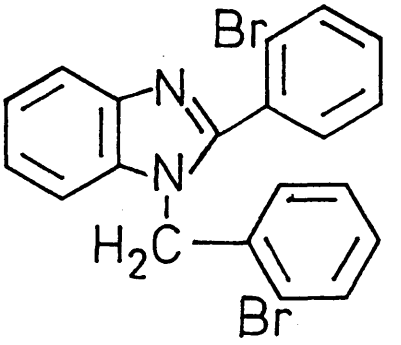

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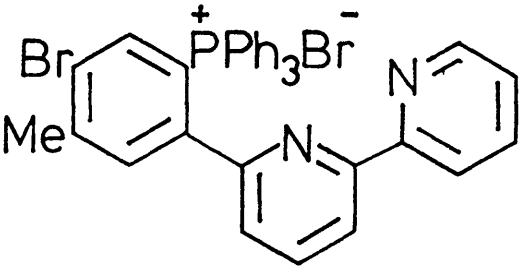

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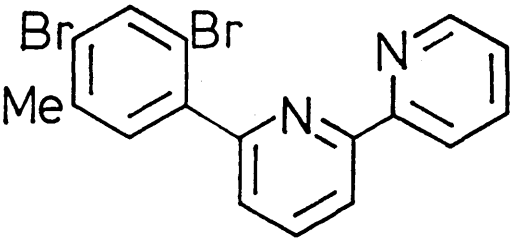

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4.2 EXPERIMENTAL DETAILS FOR THE STRUCTURE OF TRIPHENYL-2-(1-(2-BROMOBENZYL)-2-BENZIMIDAZOLYL) PHENYLPHOSPHONIUM BROMIDE

4.2.1 Crystal Data

$C_{40}H_{31}Br_2N_2Cl_6P_1$. M_r = 942.9. Triclinic, space group $\overline{P1}$, $\underline{a}$ = 11.125(6), $\underline{b}$ = 13.282(8), $\underline{c}$ = 13.947(4) Å, α= 96.78(4), β= 85.24(5), γ = 75.96(1)°, U = 1972.2Å^3, Mo-K_α λ = 0.71069Å, D_m = 1.49, D_c = 1.58 gcm^{-3}, Z = 2, μ(Mo-K_α) 24.43cm^{-1}, F(000) = 944.

4.2.2 Data Collection and Recovery

In general crystal quality was poor and great difficulty was found in selecting a suitable crystal for data collection. Eventually, a crystal of adequate quality and approximate dimensions 1.00 x 0.64 x 0.56mm was mounted with the $\underline{a}$-axis coincident with the (ω) axis of a Stöe Stadi 2 two-circle diffractometer. Data were collected using monochromated Mo-K_α radiation and the background-ω-scan background technique. Corrections for Lorentz and polarisation effects were applied but no corrections for absorption were made. The crystal was found to be weakly diffracting and of 4409 unique reflections collected from ten layers, 3137 had $I/\sigma(I) \geq 3.0$ and were used in the subsequent structure analysis.

4.2.3 Structure Determination and Refinement

Preliminary photographs showed the crystal to be triclinic and subsequent analysis confirmed the space group to be $\overline{P1}$. Interpretation of a three-dimensional

Patterson map readily afforded the positions of the two bromine atoms in the asymmetric unit. The remaining non-hydrogen atoms were located from successive electron density maps. The quality of the data prevented satisfactory location of the hydrogen atoms and all the non-hydrogen atoms except C(3) and C(46) were given anisotropic temperature factors. Scattering factors were calculated using an analytical approximation[5] and the weighting scheme adopted was: $\omega = 2.0470[\sigma^2(Fo) + 0.002519(Fo)^2]$ with $\sigma(Fo)$ from counting statistics. Full-matrix least-squares refinement gave the final $R = 0.078$ and $R' = 0.082$. Full atomic parameters are listed in Table 4.1, bond distances in Table 4.2 and angles in Table 4.3. Thermal parameters and mean planes data can be found in Tables 4.4 and 4.5 respectively.

Table 4.1 Final fractional co-ordinates ($x10^4$) with estimated standard deviations in parentheses

Atom	x	y	z
Br(1)	8 840(2)	3 689(2)	965(2)
Br(2)	7 503(2)	1 538(2)	2 156(2)
P	3 217(4)	2 325(3)	3 035(3)
N(1)	4 752(14)	4 670(12)	2 387(10)
N(2)	3 017(14)	4 916(11)	3 354(9)
C(1)	4 171(19)	4 398(13)	3 204(12)
C(2)	3 916(17)	5 426(15)	2 004(15)
C(3)	2 830(20)	5 567(15)	2 655(14)
C(4)	1 794(19)	6 257(17)	2 503(14)
C(5)	1 798(18)	6 798(16)	1 759(17)
C(6)	2 931(24)	6 643(15)	1 110(14)
C(7)	3 976(20)	5 933(16)	1 268(15)
C(8)	6 097(16)	4 276(13)	2 000(12)
C(11)	1 705(16)	2 848(14)	3 665(13)
C(12)	671(19)	2 693(15)	3 246(13)
C(13)	-488(20)	3 092(15)	3 692(15)
C(14)	-625(19)	3 619(14)	4 660(15)
C(15)	331(21)	3 723(13)	5 073(13)
C(16)	1 547(16)	3 347(14)	4 611(12)
C(21)	3 553(17)	930(15)	2 824(11)
C(22)	2 672(17)	382(17)	2 989(12)
C(23)	2 998(22)	-720(16)	2 792(13)
C(24)	4 212(23)	-1 276(16)	2 412(13)
C(25)	5 102(20)	-730(16)	2 294(12)
C(26)	4 807(21)	327(14)	2 487(12)
C(31)	3 291(16)	2 780(11)	1 881(11)
C(32)	2 332(19)	3 455(15)	1 582(13)
C(33)	2 331(19)	3 714(15)	647(15)
C(34)	3 406(22)	3 302(16)	5(13)
C(35)	4 439(20)	2 622(14)	302(14)
C(36)	4 385(18)	2 367(14)	1 223(16)
C(41)	4 334(15)	2 660(13)	3 798(10)
C(42)	4 710(15)	3 596(13)	3 748(11)
C(43)	5 657(16)	3 726(14)	4 313(13)
C(44)	6 152(17)	2 999(17)	4 963(13)
C(45)	5 720(17)	2 107(15)	5 003(12)
C(46)	4 797(16)	1 949(14)	4 408(11)
C(51)	6 827(15)	5 072(12)	2 234(12)
C(52)	8 019(18)	4 944(13)	1 814(11)
C(53)	8 708(18)	5 696(17)	1 999(14)
C(54)	8 163(21)	6 602(16)	2 598(15)
C(55)	7 019(23)	6 764(15)	3 052(14)
C(56)	6 363(18)	6 022(15)	2 875(13)
C(9)	1 563(22)	97(16)	6 285(19)
C(10)	1 752(19)	433(19)	-165(14)
CL(1)	2 638(8)	661(6)	5 717(6)
CL(2)	1 160(8)	-805(7)	5 398(7)
CL(3)	272(8)	1 073(7)	6 788(7)
CL(4)	3 306(6)	194(5)	179(4)
CL(5)	692(7)	663(7)	877(5)
CL(6)	1 474(8)	1 519(6)	-737(6)

Table 4.2 Bond distances

Bond distances in (Å) E.s.d's in parentheses

Br(1)-C(52)	1.91(2)	C(46)-C(41)	1.38(2)
C(52)-C(51)	1.37(3)	C(41)-P	1.80(2)
C(52)-C(53)	1.41(3)	P-C(11)	1.77(2)
C(53)-C(54)	1.36(3)	C(11)-C(12)	1.38(3)
C(54)-C(55)	1.33(3)	C(12)-C(13)	1.34(3)
C(55)-C(56)	1.37(3)	C(13)-C(14)	1.42(3)
C(56)-C(51)	1.41(2)	C(14)-C(15)	1.28(3)
C(51)-C(8)	1.50(3)	C(15)-C(16)	1.40(3)
C(8)-N(1)	1.49(2)	C(16)-C(11)	1.38(2)
N(1)-C(1)	1.39(2)	P-C(21)	1.78(2)
N(1)-C(2)	1.38(2)	C(21)-C(22)	1.38(3)
C(2)-C(3)	1.41(3)	C(22)-C(23)	1.41(3)
C(2)-C(7)	1.30(3)	C(23)-C(24)	1.40(3)
C(7)-C(6)	1.36(3)	C(24)-C(25)	1.37(4)
C(6)-C(5)	1.45(3)	C(25)-C(26)	1.35(3)
C(5)-C(4)	1.33(3)	C(26)-C(21)	1.44(3)
C(4)-C(3)	1.34(3)	P-C(31)	1.79(2)
C(3)-N(2)	1.38(3)	C(31)-C(32)	1.35(2)
N(2)-C(1)	1.29(2)	C(32)-C(33)	1.39(3)
C(1)-C(42)	1.42(2)	C(33)-C(34)	1.39(3)
C(42)-C(41)	1.41(3)	C(34)-C(35)	1.40(3)
C(42)-C(43)	1.40(3)	C(35)-C(36)	1.37(3)
C(43)-C(44)	1.45(3)	C(36)-C(31)	1.41(2)
C(44)-C(45)	1.39(3)		
C(45)-C(46)	1.41(3)		

Table 4.3 Bond angles

Bond angles in (°) E.s.d's ca. 2°

Br(1)-C(52)-C(51)	120	C(45)-C(46)-C(41)	121
Br(1)-C(52)-C(53)	117	C(46)-C(41)-C(42)	123
C(51)-C(52)-C(53)	123	C(46)-C(41)-P	116
C(52)-C(53)-C(54)	119	C(42)-C(41)-P	121
C(53)-C(54)-C(55)	121	C(41)-P-C(31)	114
C(54)-C(55)-C(56)	119	C(41)-P-C(21)	107
C(55)-C(56)-C(51)	124	C(41)-P-C(11)	108
C(56)-C(51)-C(52)	113	C(31)-P-C(21)	108
C(56)-C(51)-C(8)	125	C(31)-P-C(11)	110
C(52)-C(51)-C(8)	122	C(21)-P-C(11)	110
C(51)-C(8)-N(1)	113	P-C(11)-C(12)	120
C(8)-N(1)-C(1)	126	P-C(11)-C(16)	121
C(8)-N(1)-C(2)	124	C(16)-C(11)-C(12)	119
C(1)-N(1)-C(2)	110	C(11)-C(12)-C(13)	122
N(1)-C(2)-C(3)	101	C(12)-C(13)-C(14)	118
N(1)-C(2)-C(7)	135	C(13)-C(14)-C(15)	121
C(3)-C(2)-C(7)	124	C(14)-C(15)-C(16)	123
C(2)-C(7)-C(6)	118	C(15)-C(16)-C(11)	118
C(7)-C(6)-C(5)	119	P-C(21)-C(22)	123
C(6)-C(5)-C(4)	120	P-C(21)-C(26)	120
C(5)-C(4)-C(3)	121	C(26)-C(21)-C(22)	117
C(4)-C(3)-C(2)	118	C(21)-C(22)-C(23)	120
C(4)-C(3)-N(2)	130	C(22)-C(23)-C(24)	121
C(2)-C(3)-N(2)	112	C(23)-C(24)-C(25)	119
C(3)-N(2)-C(1)	107	C(24)-C(25)-C(26)	121
N(2)-C(1)-N(1)	110	C(25)-C(26)-C(21)	122
N(2)-C(1)-C(42)	124	P-C(31)-C(32)	124
N(1)-C(1)-C(42)	126	P-C(31)-C(36)	119
C(1)-C(42)-C(41)	125	C(36)-C(31)-C(32)	118
C(1)-C(42)-C(43)	120	C(31)-C(32)-C(33)	124
C(41)-C(42)-C(43)	115	C(32)-C(33)-C(34)	118
C(42)-C(43)-C(44)	123	C(33)-C(34)-C(35)	120
C(43)-C(44)-C(45)	119	C(34)-C(35)-C(36)	120
C(44)-C(45)-C(46)	118	C(35)-C(36)-C(31)	120

Table 4.4 Final Thermal Parameters ($x10^4$) with estimated standard deviations in parentheses

Anisotropic temperature factors in the form:-

$$\exp[-2\pi^2(u_{11}h^2a^{*2} + u_{22}k^2b^{*2} + u_{33}l^2c^{*2} + 2u_{12}hka^*b^* + 2u_{13}hla^*c^* + 2_{23}klb^*c^*]$$

Atom	U_{11}	U_{23}	U_{22}	U_{13}	U_{33}	U_{12}
Br(1)	516(14)	821(16)	619(14)	-252(12)	157(10)	-153(11)
Br(2)	929(19)	884(19)	843(18)	-249(14)	176(14)	-294(15)
P	471(32)	416(30)	223(26)	-71(22)	31(22)	-183(24)
N(1)	578(114)	614(113)	157(86)	-121(81)	170(85)	-340(97)
N(2)	407(108)	564(103)	332(94)	-147(82)	73(77)	-169(85)
C(1)	648(148)	367(117)	273(119)	-2(91)	116(107)	-336(111)
C(2)	435(133)	347(119)	483(139)	35(110)	65(109)	-92(103)
C(4)	671(161)	863(162)	255(120)	-1(116)	234(105)	-292(136)
C(5)	426(141)	701(153)	707(167)	-119(136)	141(124)	-154(110)
C(6)	1124(200)	392(133)	499(142)	187(107)	-508(151)	-358(138)
C(7)	833(179)	390(127)	391(137)	144(113)	-36(117)	-215(126)
C(8)	626(144)	447(119)	431(123)	-1(96)	248(103)	-295(107)
C(11)	500(133)	743(137)	427(135)	97(108)	-251(105)	-560(110)
C(12)	552(146)	802(148)	371(118)	78(106)	216(119)	-253(122)
C(13)	637(166)	724(153)	636(156)	-137(127)	-34(128)	-220(119)
C(14)	397(146)	737(154)	670(163)	-33(126)	132(119)	-288(112)
C(15)	576(161)	547(135)	486(132)	7(102)	-135(132)	-178(116)
C(16)	358(128)	749(136)	337(122)	-74(104)	-73(94)	-390(101)
C(21)	281(116)	866(146)	207(101)	-34(98)	-25(83)	-97(119)
C(22)	288(120)	967(186)	479(126)	49(116)	84(90)	-338(124)
C(23)	926(188)	475(145)	499(131)	248(113)	-185(124)	-467(133)
C(24)	826(175)	543(139)	508(136)	-181(110)	96(122)	-268(145)
C(25)	802(162)	531(154)	390(125)	120(107)	145(106)	-89(132)
C(26)	1156(203)	244(125)	445(126)	38(94)	20(122)	-311(123)
C(31)	446(116)	85(85)	305(103)	101(81)	-250(102)	-136(82)
C(32)	749(153)	586(134)	254(128)	105(100)	-142(103)	-347(123)
C(33)	654(154)	808(154)	443(146)	292(123)	-120(122)	-275(120)
C(34)	925(175)	632(143)	285(120)	250(110)	-155(135)	-278(129)
C(35)	863(166)	361(120)	263(129)	76(94)	59(109)	-343(119)
C(36)	508(138)	476(126)	668(158)	-5(116)	189(117)	-107(100)
C(41)	499(117)	563(125)	133(93)	-30(90)	112(80)	-211(102)
C(42)	352(116)	491(122)	279(105)	-195(88)	220(88)	-159(92)
C(43)	282(111)	571(134)	569(130)	-50(112)	-96(100)	-180(96)
C(44)	481(128)	656(153)	397(126)	-310(116)	-40(100)	30(119)
C(45)	703(138)	495(129)	279(112)	-112(96)	5(95)	-128(110)
C(51)	354(119)	245(109)	390(110)	50(91)	65(93)	43(88)
C(52)	670(150)	340(115)	264(109)	-28(88)	72(103)	27(108)
C(53)	516(137)	599(146)	697(150)	-26(127)	-19(110)	-265(122)
C(54)	672(165)	653(161)	715(150)	-32(129)	-30(127)	-516(127)
C(55)	891(189)	489(139)	604(141)	-36(110)	-106(135)	-352(134)
C(56)	546(134)	558(141)	592(135)	-74(119)	170(107)	-154(119)

Table 4.4 (continued)

Atom	U_{11}	U_{23}	U_{22}	U_{13}	U_{33}	U_{12}
C(9)	1176(200)	561(144)	1527(226)	-398(148)	520(173)	-460(139)
C(10)	665(158)	1285(205)	637(146)	14(143)	193(116)	-303(142)
CL(1)	1684(71)	1096(54)	1277(59)	-115(45)	290(53)	-552(51)
CL(2)	1395(71)	1423(69)	2021(90)	-423(64)	-186(63)	-361(55)
CL(3)	1355(70)	1798(81)	1701(79)	-780(65)	270(58)	-346(59)
CL(4)	873(46)	1466(58)	880(44)	-180(40)	-130(35)	-405(41)
CL(5)	1029(55)	2807(101)	895(49)	-771(57)	301(40)	-987(60)
CL(6)	1593(74)	1112(60)	1630(74)	0(55)	-467(59)	-343(52)

Isotropic temperature factors in the form:-

$$\exp[-U \sin^2\theta/\lambda^2]$$

C(46)	656(64)
C(3)	472(50)

Table 4.5 Deviations from selected least squares mean planes for triphenyl-2-(1-(2-bromobenzyl)-2-benzimidazolyl)) phenylphosphonium bromide. Deviations in parentheses [ ] are for atoms not included in the calculation of the plane.

Plane A

C(11)-C(16)

C(11), 0.025(9); C(12), 0.028(9); C(13), 0.012(1);
C(14), 0.007(9); C(15), -0.010(1); C(16), -0.007(0);
P,[-0.004(3)]

Plane B

C(21)-C(26)

C(21), 0.023(1); C(22), -0.007(0); C(23), -0.017(5);
C(24), 0.025(8); C(25), -0.009(0); C(26), -0.015(5);
P, [0.063(9)]

Plane C

C(31)-C(36)

C(31), 0.016(0); C(32), -0.019(9); C(33), 0.010(2);
C(34), 0.002(4); C(35), -0.005(7); C(36), -0.003(0);
P, [0.179(9)]

Plane D

C(41)-C(46)

C(41), 0.021(1); C(42), -0.022(8); C(43), 0.018(7);
C(44), -0.003(7); C(45), -0.007(2); C(46), 0.002(8);
P, [0.105(3)]

Table 4.5 (continued)

Plane E

C(2)-C(7)

C(2), 0.003(3); C(3), -0.006(2), C(4), 0.002(3);
C(5), 0.004(3); C(6), -0.007(5); C(7), 0.003(7);
N(1),[0.014(8)]; N(2), [0.046(2)]

Plane F

C(1), N(1), N(2), C(2), C(3), C(4), C(5), C(6), C(7).
C(1), -0.006(6); N(1), 0.000(4); N(2), 0.022(4);
C(2), -0.003(8); C(3), -0.019(7); C(4), -0.006(2);
C(5), 0.006(2); C(6), 0.000(5); C(7), 0.006(7);
C(8), [-0.076(1)]; C(42), [0.087(3)]

Plane G

C(8), C(51), C(52), C(53), C(54), C(55), C(56), Br(1)
C(8), 0.039(1); C(51), -0.004(5); C(52), 0.004(9);
C(53), 0.008(9); C(54), 0.037(3); C(55), -0.020(5);
C(56), -0.036(4); Br(1), -0.029(0); N(1), [0.290(2)]

Angles (°) between least squares planes

A/B	61.4	B/D	62.8	C/G	89.3
A/C	130.3	B/E	56.0	D/E	66.2
A/D	92.2	B/F	55.6	D/F	66.0
A/E	117.0	B/G	23.1	D/G	79.8
A/F	116.6	C/D	78.6	E/F	0.4
A/G	41.2	C/E	16.9	E/G	76.1
B/C	71.4	C/F	17.3	F/G	75.7

Table 4.5 (continued)

Least squares planes equations of the form

$aX + bY + cZ - d = 0$

Plane	a	b	c	d
A	0.1199	0.9272	-0.3548	1.3037
B	-0.2857	0.1942	-0.9384	-4.8527
C	-0.5934	-0.7414	-0.3133	-6.0386
D	0.5497	-0.3945	-0.7364	-1.5508
E	-0.5015	-0.6455	-0.5761	-9.0282
F	-0.5006	-0.6408	-0.5821	-9.0011
G	-0.3111	0.5569	-0.7701	-1.9170

4.3 DISCUSSION OF THE STRUCTURE OF TRIPHENYL-2-(1-BROMOBENZYL)-2-BENZIMIDAZOLYL)PHENYLPHOSPHONIUM BROMIDE

While crystal quality precludes a detailed discussion of the structure of the phosphonium cation, the following features are, nevertheless, noteworthy. The structure clearly shows that the halogen of the 2-(ortho-bromophenyl) substituent attached to the benzimidazole ring system has been replaced by phosphorus, as would be expected as a result of its orientation with respect to the pyridine-like nitrogen of the benzimidazole system, which is the effective template donor atom. It has also been established that the phosphorus atom occupies a slightly distorted tetrahedral environment (Table 4.3) in which the three phenyl rings exhibit a characteristic propeller geometry (Fig 4.1). As expected, the benzimidazole ring system is planar (the dihedral angle between C(2)-C(7) mean plane and the C(1), N(1), C(2), C(3), N(2) mean plane is 0.44°). In contrast the C(41)-C(46) ring and the other substituent ring C(51)-C(56) are not co-planar with respect to the benzimidazole system, the dihedral angles between them and the benzimidazole system being 66° and 75° respectively. This twisting of the substituent rings would appear to reflect an attempt at minimising any possible interactions between:-

(i) the benzimidazole system and the C(31)-C(36) ring.

(ii) the bromine atom on C(52) with any of its neighbours, especially those on the C(41)-C(46) ring.

Angles and bond lengths in this 1,2-disubstituted benzimidazole

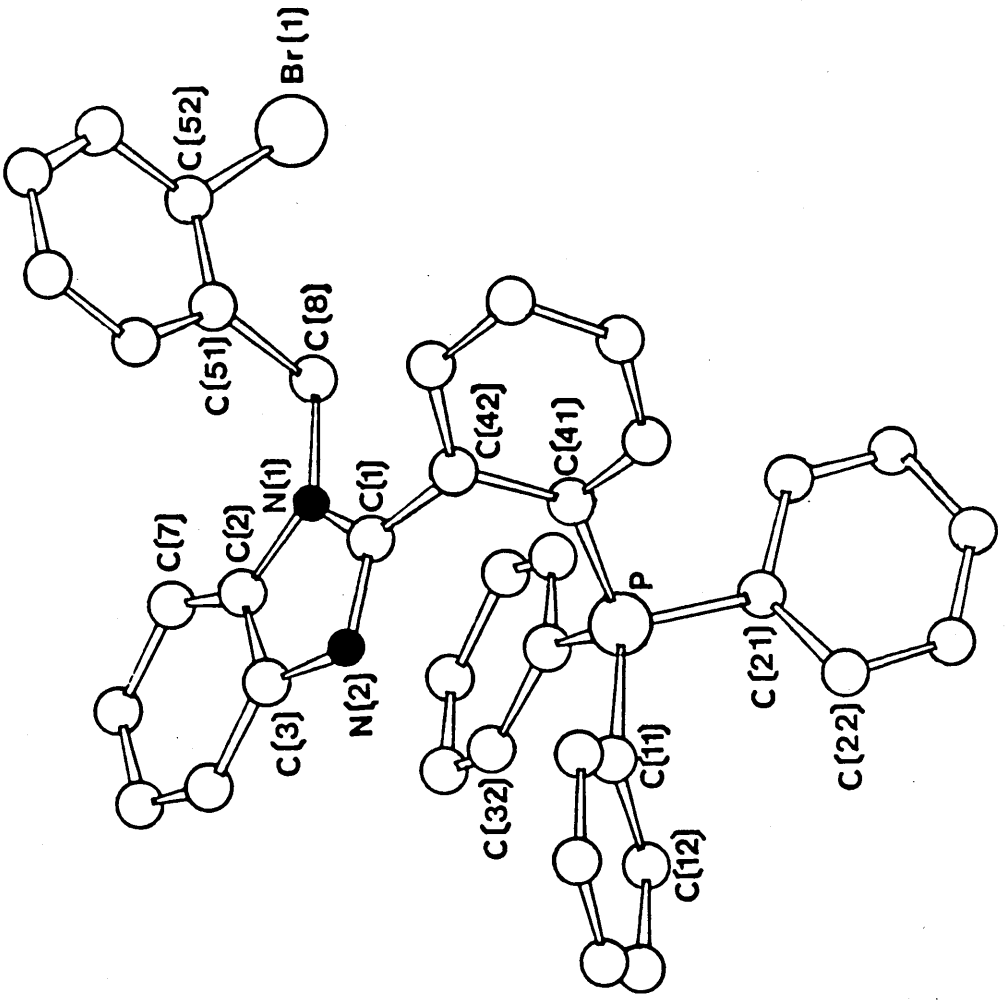

Figure 4.1 X-Ray structure of Triphenyl-2-(1-(2-bromobenzyl)-2-benzimidazolyl) phenylphosphonium bromide

compare well with the literature values for the crystal structure of benzimidazole[6].

One important feature worth comment is that the benzimidazole ring is inclined to the C(41)-C(46) phenyl ring such that the nitrogen atom N(2) is closely approached by the phosphorus atom. A N(2)-P bond length of 3.37Å seems to suggest that the formation of a nitrogen-phosphorus ($N:\longrightarrow P^+$) bond is possible, since the bond distance lies within the sum of the covalent radii (N-P bond 3.4Å)[7].

There does not appear to be any significant interaction between the bromide ion and the phosphonium cation, the closest $P^+ \ldots\ldots Br^-$ distance being 4.5Å.

For purposes of clarity, two chloroform molecules have been omitted from the crystal structure. It is thought that the hydrogen atoms from these two molecules are hydrogen bonded to the bromide anion [bond distances are Br(2)-H(9) 2.30 and Br(2)-H(10) 2.55Å respectively], and that these molecules in turn form discrete channels running through the crystal lattice.

4.4 EXPERIMENTAL DETAILS FOR THE STRUCTURE OF 3-(2-TRIPHENYLPHOSPHONIO-4-BROMO-5-METHYL-PHENYL)2,2′-BIPYRIDYL BROMIDE

4.4.1 Crystal Data

$C_{35}H_{31}Br_2N_2O_2P_1$. M_r = 701.8. Monoclinic, space group $P2_1/c$, $\underline{a}$ = 8.743(5), $\underline{b}$ = 22.398(4), $\underline{c}$ = 15.669(3)Å, $\underline{\beta}$ = 94.0(0), $\underline{\alpha}$ = $\underline{\gamma}$ = 90°. U = 3061.2Å^3, Mo-K_α λ = 0.71069Å, D_m = 1.52, D_c = 1.54 gcm^{-3}, Z = 2, μ(Mo-K_α) 13.25 cm^{-1}, F(000) = 712.

4.4.2 Data Collection and Recovery

Intensities were measured for a crystal, approximate dimensions 0.20 x 0.12 x 0.12 mm, mounted on a glass fibre rod with the c axis coincident with the rotation (ω) axis of a two-circle Stöe Stadi 2 diffractometer Monochromatic Mo-K_α radiation was used and the background-ω-scan background technique employed. Sixteen layers were collected giving 3169 independent reflections, of which 1704 had $I \geq 3\sigma(I)$ and were used for subsequent analysis. Corrections were applied as above.

4.4.3 Structure Determination and Refinement

The space group and unit cell parameters were obtained from oscillation and Weissenberg photographs. Systematic absences when hOl, l = 2n + 1 and OkO, k = 2n + 1, and density measurements indicate that the space group is $P2_1/c$. The approximate positions of the two bromine atoms were calculated using a three-dimensional Patterson synthesis.

Multisolution direct methods using SHELX[8] enabled the position of all non-hydrogen atoms to be readily located. Scattering factors were calculated using an analytical approximation[5] and the weighting scheme $\omega = 1.000[\sigma^2(Fo) + 0.001265(Fo)^2]$ adopted. Full-matrix least-squares refinement for the ordered non-hydrogen atoms gave final $R = 0.0951$ and $R' = 0.0958$. Full atomic parameters are listed in Table 4.6, bond distances in Table 4.7, and bond angles in Table 4.8. A list of thermal parameters and mean planes data can be found in Tables 4.9 and 4.10 respectively.

Table 4.6 Final fractional co-ordinates ($x10^4$) with estimated standard deviations in parentheses.

Atom	x	y	z
Br(1)	6 978(3)	3 399(1)	3 677(1)
Br(2)	-981(6)	1 063(3)	6 808(3)
P	3 064(6)	3 817(2)	6 213(3)
N(1)	3 962(16)	2 898(7)	7 571(10)
N(2)	1 861(18)	3 014(8)	9 451(11)
C(11)	2 339(22)	4 270(9)	5 315(12)
C(12)	2 911(24)	4 837(11)	5 169(16)
C(13)	2 310(29)	5 173(11)	4 493(17)
C(14)	1 249(29)	4 939(12)	3 953(16)
C(15)	698(26)	4 376(12)	4 062(16)
C(16)	1 223(21)	4 039(9)	4 744(14)
C(21)	1 425(21)	3 496(9)	6 656(12)
C(22)	770(22)	3 705(8)	7 350(12)
C(23)	-499(24)	3 432(12)	7 667(14)
C(24)	-1 060(25)	2 940(12)	7 289(16)
C(25)	-407(22)	2 674(10)	6 601(14)
C(26)	916(22)	2 972(11)	6 273(13)
C(31)	4 105(24)	4 282(9)	6 935(12)
C(32)	3 430(26)	4 819(12)	7 237(13)
C(33)	4 260(28)	5 197(12)	7 792(16)
C(34)	5 670(32)	5 094(10)	8 007(13)
C(35)	6 405(27)	4 577(11)	7 706(14)
C(36)	5 596(26)	4 174(9)	7 155(12)
C(41)	4 380(19)	3 272(8)	5 794(11)
C(42)	5 020(20)	3 458(9)	5 044(12)
C(43)	6 101(22)	3 098(9)	4 682(12)
C(44)	6 472(22)	2 561(11)	4 979(13)
C(45)	5 814(21)	2 366(9)	5 729(12)
C(46)	4 767(20)	2 719(9)	6 144(13)
C(51)	4 136(24)	2 508(10)	6 943(14)
C(52)	3 660(25)	1 915(11)	6 997(14)
C(53)	2 920(27)	1 697(10)	7 678(16)
C(54)	2 728(22)	2 093(10)	8 298(16)
C(55)	3 255(20)	2 694(9)	8 264(12)
C(61)	2 958(24)	3 116(10)	8 976(14)
C(62)	3 792(26)	3 624(11)	9 015(13)
C(63)	3 553(27)	4 088(11)	9 610(15)
C(64)	2 355(28)	3 976(10)	10 097(14)
C(65)	1 586(24)	3 416(10)	10 001(14)
C(7)	7 546(22)	2 140(9)	4 567(13)
O(1)	7(17)	15(12)	6 435(13)
O(2)	-2 428(35)	543(11)	4 981(18)

Table 4.7 Bond distances

Bond distances in (Å) E.s.d's in parentheses

C(41)-C(42)	1.39(3)	P-C(11)	1.81(2)
C(42)-C(43)	1.39(3)	P-C(21)	1.79(2)
C(43)-Br(1)	1.92(2)	P-C(31)	1.75(2)
C(43)-C(44)	1.32(3)	P-C(41)	1.83(2)
C(44)-C(7)	1.51(3)	C(11)-C(12)	1.39(3)
C(44)-C(45)	1.40(3)	C(12)-C(13)	1.37(4)
C(45)-C(46)	1.40(3)	C(13)-C(14)	1.32(4)
C(46)-C(41)	1.39(3)	C(14)-C(15)	1.36(4)
C(46)-C(51)	1.48(3)	C(15)-C(16)	1.36(2)
C(51)-C(52)	1.40(3)	C(16)-C(11)	1.38(3)
C(52)-C(53)	1.38(3)	C(21)-C(22)	1.35(3)
C(53)-C(54)	1.34(3)	C(22)-C(23)	1.39(3)
C(54)-C(55)	1.43(3)	C(23)-C(24)	1.33(4)
C(55)-N(1)	1.36(2)	C(24)-C(25)	1.39(3)
N(1)-C(51)	1.33(3)	C(25)-C(26)	1.46(3)
C(55)-C(61)	1.50(3)	C(26)-C(21)	1.38(3)
C(61)-C(62)	1.35(3)	C(31)-C(32)	1.44(3)
C(62)-C(63)	1.42(3)	C(32)-C(33)	1.38(3)
C(63)-C(64)	1.36(3)	C(33)-C(34)	1.28(4)
C(64)-C(65)	1.43(3)	C(34)-C(35)	1.42(3)
C(65)-N(2)	1.28(3)	C(35)-C(36)	1.41(3)
N(2)-C(61)	1.28(3)	C(36)-C(31)	1.35(3)

Table 4.8 Bond angles

Bond angles in (°) E.s.d's ca. 2°

P-C(41)-C(42)	114	P-C(11)-C(12)	122
P-C(41)-C(46)	127	P-C(11)-C(16)	119
C(46)-C(41)-C(42)	120	C(16)-C(11)-C(12)	119
C(41)-C(42)-C(43)	119	C(11)-C(12)-C(13)	120
C(42)-C(43)-C(44)	123	C(12)-C(13)-C(14)	119
C(42)-C(43)-BR(1)	117	C(13)-C(14)-C(15)	122
C(44)-C(43)-BR(1)	121	C(14)-C(15)-C(16)	121
C(43)-C(44)-C(45)	118	C(15)-C(16)-C(11)	119
C(43)-C(44)-C(7)	124	P-C(21)-C(22)	125
C(45)-C(44)-C(7)	118	P-C(21)-C(26)	115
C(44)-C(45)-C(46)	122	C(26)-C(21)-C(22)	120
C(45)-C(46)-C(41)	118	C(21)-C(22)-C(23)	122
C(45)-C(46)-C(51)	120	C(22)-C(23)-C(24)	119
C(41)-C(46)-C(51)	122	C(23)-C(24)-C(25)	123
C(46)-C(51)-C(52)	119	C(24)-C(25)-C(26)	117
C(46)-C(51)-N(1)	119	C(25)-C(26)-C(21)	118
C(52)-C(51)-N(1)	122	P-C(31)-C(32)	120
C(51)-C(52)-C(53)	123	P-C(31)-C(36)	121
C(52)-C(53)-C(54)	115	C(36)-C(31)-C(32)	119
C(53)-C(54)-C(55)	123	C(31)-C(32)-C(33)	121
C(54)-C(55)-N(1)	121	C(32)-C(33)-C(34)	121
C(54)-C(55)-C(61)	120	C(33)-C(34)-C(35)	121
C(61)-C(55)-N(1)	120	C(34)-C(35)-C(36)	121
C(55)-N(1)-C(51)	117	C(35)-C(36)-C(31)	119
C(55)-C(61)-C(62)	117	C(11)-P-C(21)	106
C(55)-C(61)-N(2)	120	C(11)-P-C(31)	108
C(62)-C(61)-N(2)	123	C(11)-P-C(41)	107
C(61)-C(62)-C(63)	123	C(21)-P-C(31)	113
C(62)-C(63)-C(64)	113	C(21)-P-C(41)	114
C(63)-C(64)-C(65)	119	C(31)-P-C(41)	109
C(64)-C(65)-N(2)	125		
C(65)-N(2)-C(61)	117		

Table 4.9 Final thermal parameters (x10^4) with estimated standard deviations in parentheses.

Anisotropic temperature factors in the form:-

$$\exp[-2\pi^2(u_{11}h^2a^{*2} + u_{22}k^2b^{*2} + u_{33}l^2c^{*2} + 2u_{12}hka^*b^* + 2u_{13}hla^*c^* + 2_{23}klb^*c^*]$$

Atom	U_{11}	U_{23}	U_{22}	U_{13}	U_{33}	U_{12}
Br(1)	487(14)	685(18)	463(15)	-16(17)	211(11)	-31(17)
Br(2)	2247(53)	2475(61)	1242(38)	12(39)	250(36)	-1101(48)
P	306(32)	312(33)	228(34)	-30(32)	39(27)	37(32)
C(11)	169(115)	224(129)	231(124)	-25(113)	-7(106)	159(106
C(12)	349(135)	415(165)	666(188)	130(162)	62(131)	-155(139
C(13)	531(167)	459(161)	524(166)	155(180)	61(144)	25(162
C(14)	464(158)	695(222)	374(157)	245(156)	-18(135)	56(151
C(15)	463(161)	503(181)	520(178)	-39(163)	37(141)	-45(151
C(16)	203(128)	291(137)	395(144)	-8(136)	-88(118)	173(112
C(21)	308(127)	232(138)	228(125)	100(116)	-89(104)	-21(109
C(23)	435(157)	565(174)	372(148)	167(162)	-31(121)	70(152
C(24)	239(138)	711(205)	506(177)	249(168)	161(138)	135(147
C(25)	321(147)	485(164)	420(155)	240(134)	-134(130)	108(127
C(26)	191(130)	671(184)	347(145)	201(145)	170(117)	257(129
C(31)	253(135)	376(144)	279(130)	-31(125)	-102(107)	-49(120
C(32)	559(161)	713(187)	188(124)	0(147)	-34(121)	-301(175
C(33)	313(145)	622(180)	701(193)	328(181)	-10(139)	290(163
C(34)	823(203)	397(166)	203(132)	-56(129)	-79(135)	-328(164
C(35)	599(166)	411(157)	394(152)	130(136)	75(137)	177(144
C(36)	515(165)	303(138)	234(127)	-97(120)	-79(118)	-131(129
C(41)	158(104)	245(135)	227(118)	-104(109)	-53(91)	-106(100
C(44)	243(124)	844(196)	307(137)	-298(143)	51(109)	-45(128
C(46)	176(116)	262(135)	476(150)	-53(122)	-129(107)	-8(102
C(51)	427(145)	344(150)	615(166)	212(154)	222(127)	-4(126
C(52)	575(169)	628(183)	227(143)	-104(140)	-80(130)	151(147
C(53)	1002(208)	205(142)	582(178)	-246(154)	246(163)	-91(151
C(54)	378(144)	445(161)	569(173)	293(157)	-4(132)	65(133
C(62)	964(185)	1095(215)	701(161)	300(154)	435(146)	357(160
C(64)	831(191)	395(168)	258(134)	-43(134)	-65(137)	465(150
C(65)	607(164)	393(154)	507(159)	128(164)	-2(128)	309(151
O(1)	281(93)	3092(297)	1358(175)	1801(202)	-236(107)	-97(138
O(2)	2563(306)	1244(210)	2161(285)	232(203)	-1038(253)	-504(221

Isotropic temperature factors in the form:-

$$\exp[-U \sin^2\theta/\lambda^2]$$

N(1)	220(40)	C(45)	316(55)
N(2)	117(43)	C(55)	260(52)
C(22)	258(52)	C(61)	340(59)
C(42)	269(49)	C(63)	487(65)
C(43)	281(54)		

Table 4.10 Deviations from selected least mean planes for 3-(2-triphenylphosphonio-4-bromo-5-methylphenyl)2,2'-bipyridyl bromide. Deviations in parentheses [ ] are for atoms not included in the calculation of the plane.

Plane A

C(11)-C(16)

C(11), -0.011(1); C(12), 0.021(6); C(13),-0.015(8);
C(14), -0.000(9); C(15), 0.011(6); C(16),-0.005(4);
P, [-0.003(6)]

Plane B

C(21)-C(26)

C(21), 0.026(3); C(22), -0.019(0); C(23), -0.004(1);
C(24), 0.018(4); C(25), -0.010(1); C(26), -0.011(6);
P, [-0.001(1)]

Plane C

C(31)-C(36)

C(31), -0.017(9); C(32), 0.020(6); C(33), -0.012(6);
C(34), 0.001(2); C(35), 0.001(7); C(36), 0.007(1);
P, [0.067(2)]

Plane D

C(41), C(42), C(43), Br(1), C(44), C(7), C(45), C(46)
C(41), 0.007(6); C(42), 0.043(7); C(43), -0.016(7);
Br(1), -0.027(2); C(44), -0.004(0); C(7), 0.035(5);
C(45), -0.020(7); C(46), -0.018(1); P, [0.002(2)];
C(51), [-0.076(9)]

Plane E

C(51)-C(55), N(1)

C(51), 0.013(5); C(52), -0.013(8); C(53), 0.002(5);

C(54), 0.008(9); C(55), -0.009(2); N(1), -0.001(9);

C(46), [0.145(4)]; C(61), [0.036(1)]

Plane F

C(61)-C(65), N(2)

C(61), -0.000(9); C(62), 0.007(4); C(63), -0.016(6);

C(64), 0.020(4); C(65), -0.014(9); N(2), 0.004(6);

C(55), [0.149(0)]

Angles (°) between least squares planes

A/B	106.8	B/C	54.6	C/E	78.2
A/C	60.7	B/D	57.3	C/F	56.1
A/D	94.0	B/E	25.1	D/E	40.6
A/E	119.5	B/F	7.8	D/F	50.0
A/F	103.5	C/D	89.7	E/F	22.1

Least squares planes equations of the form.

$$aX + bY + cZ - d = 0$$

Plane	a	b	c	d
A	0.7451	-0.3760	-0.5509	-7.0712
B	-0.5701	0.5427	-0.6168	-2.4891
C	0.3295	0.5137	-0.7922	-2.7101
D	-0.7179	-0.4037	-0.5672	-10.3973
E	-0.8563	0.2645	-0.4437	-5.7891
F	-0.5994	0.4255	-0.6779	-7.5029

4.5 DISCUSSION OF THE STRUCTURE OF 3-(2-TRIPHENYL-PHOSPHONIO-4-BROMO-5-METHYLPHENYL)2,2'-BIPYRIDYL BROMIDE

Although it has not proved possible to gain detailed structural data for this phosphonium salt, it is quite clear that the bromine atom in the ortho-position with respect to the bipyridyl system has been replaced by phosphorus, and that the para-bromine atom contained in the same aryl ring remains unaffected.

The geometry around the phosphorus atom (Fig. 4.2) is approximately tetrahedral, with the bond angles ranging from 106-114° (Table 4.8). As expected, the phenyl ring C(41)-C(46) is effectively planar with Br(1), C(7) and C(51) atoms. Mean plane data also identified the remaining phenyl groups C(11)-C(16), C(21)-C(26) and C(31)-C(36) as being planar. Both pyridine rings, of the bipyridyl system, are planar and are inclined to one another at an angle of 22.1°. The twisting of these rings to each other might be explained by the accommodation of the large triphenylphosphine group.

Again an important feature worth noting in this crystal structure is that the pyridine ring C(51)-C(55) is inclined to the C(41)-C(46) phenyl ring so that the overall configuration is such that the nitrogen atom N(1) is closely approached by the phosphorus atom, giving a N(1)-P distance of 3.03Å, which is within the sum of their Van der Waal's radii (N = 1.55, P = 1.85Å)[7]. Such an interaction between N(1) and P may also be indicated

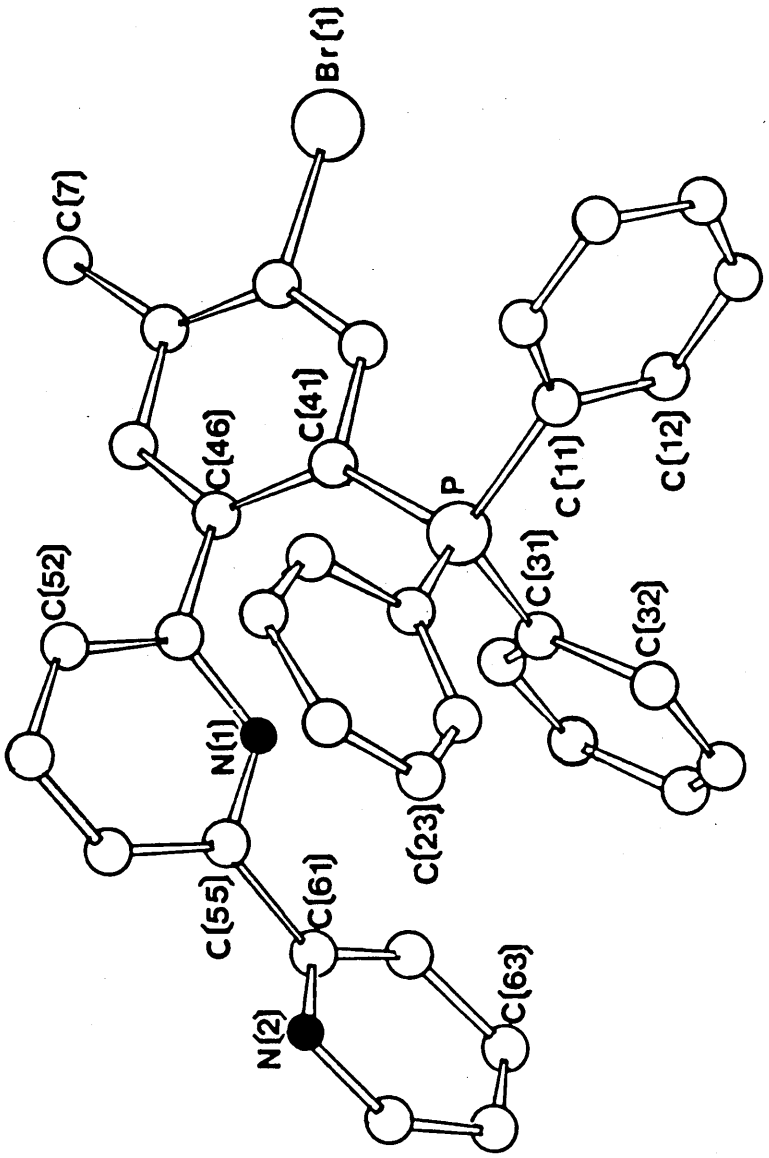

Figure 4.2 X-Ray structure of 3-(2-Triphenylphosphonio-4-bromo-5-methylphenyl)2,2´-bipyridyl bromide

by the increase in the P - C(41)-C(46) bond angle to 127.0° (compared to the other exocyclic angle P - C(41)-C(42), 114.1°).

Positions for the anionic bromide Br(2) and two oxygen atoms O(1) and O(2) were identified and have subsequently been omitted from the crystal structure for clarity. No other atoms were identified as associating with the oxygen atoms and although no hydrogen atoms would be located on these atoms, it is believed that they are water molecules entrapped in the crystal lattice (confirmed by microanalysis). Although the bromide anion Br(2) shows no sign of interaction with the cation, ($P^+....Br^-$ 4.6Å), it has been located within the sum of the Van der Waal's radii (Br....O = 3.35Å) for both O(1)-Br(2), 2.58Å and O(2)-Br(2), 3.27Å.

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COURSES AND CONFERENCES ATTENDED

1. Applications of N.M.R. Spectroscopy to Inorganic Chemistry, 10 x 1 hour lectures, Sheffield University, January 1985.

2. Homogeneous Catalysis by transition Metal Compounds, 10 x 1 hour lectures, Sheffield University, January 1985.

3. Molecular Receptors, 10 x 1 hour lectures, Sheffield University, January 1985.

4. The First Firth Inorganic Symposium, 1 day conference, Sheffield University, March 1985.

5. The Second Firth Inorganic Symposium, 1 day conference, Sheffield University, March 1986.

Further Studies of the Kinetic Template Effect in the Metal Ion-catalysed Reactions of *ortho*-Donor-substituted Aryl Halides with Tertiary Phosphines. Structural Requirements of the Template

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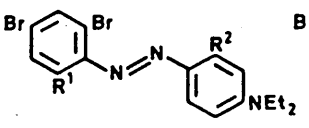
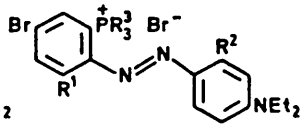
The reactions of a series of Schiff's bases, derived from *ortho*-chloro-, bromo- or iodo-benzaldehydes and *p*-anisidine, with tertiary phosphines in the presence of nickel(II) bromide in refluxing ethanol proceed with displacement of the *ortho*-halogen to form the related *ortho*-substituted arylphosphonium salts. These reactions appear to be examples of a kinetic template effect in which the Schiff's base moiety aids the catalytic role of the metal ion in promoting the substitution reaction. Introduction of a second donor atom into the substituent group present at the nitrogen of related Schiff's bases inhibits the reactions due to diversion of the metal ion in other modes of co-ordination. The reactions are also inhibited by steric crowding at the imino-nitrogen. A range of other aryl halides bearing *ortho*-substituents having the potential to act as co-ordination templates has been prepared and their reactions with phosphines in the presence of metal ions studied enabling the rather critical nature of effective template groups to be defined. Detailed ^{13}C n.m.r. data are also reported for the Schiff's bases and related arylphosphonium salts.

The formation of arylphosphonium salts from the reactions of tertiary phosphines with aryl halides normally only proceeds at elevated temperature (150—200 °C) in the presence of a transition metal salt, *e.g.* cobalt(II) bromide or nickel(II) bromide, usually in the absence of a solvent.[1–4] In recent work,[5,6] we have shown that when the *o*-bromodiarylazo dyestuffs (**1**; R^1 = H or Me, R^2 = H or NHAc) are heated under reflux in ethanol with a range of tertiary phosphines (2 mol equiv.) in the presence of copper(II) acetate or nickel(II) bromide (0.1 mol equiv.), the related diarylazophosphonium salts (**2**; R^1 = H or Me, R^2 = H or NHAc, R^3 = *e.g.*, Bu, Ph, 2-thienyl or 2-furyl) are formed in good yield. These reactions proceed under mild conditions with complete regiospecific replacement of the halogen *ortho* to the azo group. The *para*-halogen is unaffected. Replacement of the *ortho*-halogen does not occur in the absence of the metal salt catalyst. We have suggested that these reactions involve the operation of a kinetic template effect in which metal ion-promoted replacement of the halogen *ortho* to the azo group is assisted by co-ordination of the metal to an azo nitrogen atom. A related regiospecific replacement under mild conditions occurs in the reaction of triethylphosphite with the dyestuffs (**1**) in the presence of copper(II) acetate, to give related *o*-diarylazophosphonate ester.[7] The mechanism of these phosphonation reactions has been studied in detail and found to be rather complex.[8]

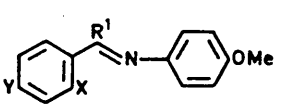


(**1**)

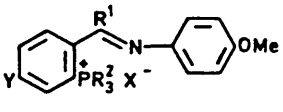


(**2**)

In order to extend our study of the operation of such kinetic template effects in promoting the formation of aryl–phosphorus bonds, we have explored the reaction towards tertiary phosphines of a range of aryl halides bearing substituents in the *ortho* position which have the potential to co-ordinate to a metal ion catalyst and perhaps to promote facile replacement of the halogen under mild conditions.



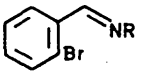
(**3**)



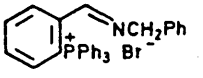
(**4**)

Initial studies[5] centered on a series of Schiff's bases of type (**3**; R^1 = H, X = Cl, Br, or I; Y = H or Cl) derived from the reactions of halogenobenzaldehydes and *p*-anisidine. On treatment with tributylphosphine or triphenylphosphine (2 mol) in refluxing ethanol in the presence of nickel(II) bromide (0.1 mol), the salts (**4**) are formed over several hours. Preliminary comparative rate studies using a conductimetric technique indicate that the ease of replacement of the *ortho* halogen is I < Br < Cl. The related *o*-fluoro Schiff's bases do not undergo the reaction. The isomeric *p*-halocompounds (**3**; R^1 = H; X = H; Y = Cl, Br, or I) also do not react under these conditions. The dichloro Schiff's base (**3**; R^1 = H; X = Y = Cl) undergoes a regiospecific replacement of the *ortho*-chlorine to give the salts (**4**; R^1 = H; R^2 = Bu or Ph; X = Y = Cl). Unambiguous proof that the *ortho*-chlorine is replaced is provided by alkaline hydrolysis of the tributylphosphonium salt, which proceeds with cleavage from phosphorus of the group most stable as a carbanion[9,10] to give the *para*-chloro Schiff's base (**3**; R^1 = H, X = H; Y = Cl). The above reactions also proceed in acetonitrile and in methanol, but at a slower rate than in ethanol, and also to some extent in tetrahydrofuran and in chloroform. No reactions occur in the absence of the nickel(II) halide, and as the concentration of this catalyst increases, so does the rate of formation of the phosphonium salt. The reaction of equimolar amounts of preformed bis(phosphine)nickel(II) halide complexes with the *o*-halogeno Schiff's bases leads to a much faster rate of formation of the phosphonium salts. Apart from nickel(II), no other metal ion has been found which significantly catalyses these reactions. In particular, no salt formation was observed when copper(II) acetate was used as the catalyst, in marked contrast to the related reactions of the dyestuffs (**1**).

The related Schiff's base (**3**; R^1 = Me; X = Br; Y = H),

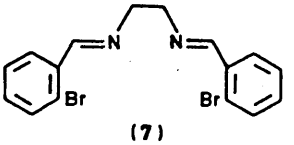


(5)

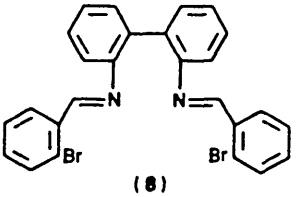


(6)

derived from the reaction of *o*-bromoacetophenone with *p*-anisidine in toluene, also undergoes the replacement reaction to give the salts (4; R^1 = Me; R^2 = Ph; X = Br; Y = H), the presence of the methyl group on the azomethine carbon causing no steric effect. However, increased steric crowding at the azomethine nitrogen is found to inhibit the reaction. Thus whereas the Schiff's base (5; R = CH_2Ph) reacts with triphenylphosphine in the presence of nickel(II) bromide to give the salt (6), the related Schiff's bases [5; R = CH(Me)Ph or Bu^t] fail to undergo the reaction. Introduction of a second donor site in the imino moiety of the Schiff's base also inhibits the reaction. Thus the Schiff's bases (5; R = CH_2CH_2OH, 2-pyridylethyl, 2-benzothiazolyl, or 2-benzimidazolyl) all fail to undergo the substitution reaction on heating with triphenylphosphine in ethanol containing *either* a catalytic quantity of nickel(II) bromide *or* in the presence of an equimolar amount of a preformed bis(phosphine)nickel(II) halide complex. It would seem that under these conditions, metal ion-promoted hydrolysis of the Schiff's base predominates, to give the aldehyde and free amino compound. These results imply that when the Schiff's base bears a second donor group which is capable of co-ordinating with the metal ion, especially when the formation of a chelate complex is possible, then the metal ion is diverted from its catalytic role. Support for this view is found in the reactions of the *o*-halogenoaryl Schiff's bases (7) and (8), derived from α,ω-diamines. These compounds have the potential to form



(7)

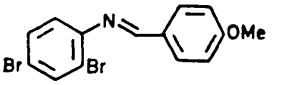


(8)

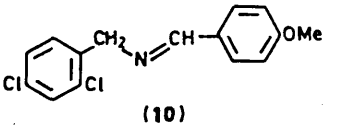
respectively five- and seven-membered ring chelate complexes with the metal ion, and do not undergo the substitution reaction on treatment with a tertiary phosphine in the presence of nickel(II) bromide. Instead, it is found that these substrates undergo hydrolysis to form 2-bromobenzaldehyde and the respective diamine.

The very critical nature of the donor atom and its position with respect to the *ortho*-halogen for the promotion of a template-assisted replacement reaction is illustrated by studies of the reactivity of a number of related systems. Thus both Schiff's base system (9) and (10) fail to undergo conversion to phosphonium salts, presumably because neither is able to be involved in the appropriate mode of metal co-ordination (*e.g.* the formation of a five-membered ring involving the nitrogen and the *ortho*-halogen) to promote the reactions leading to replacement of the *ortho*-halogen. The oxime (11) and semicarbazone (12) are similarly unreactive.

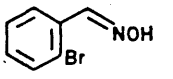
The *o*-halogenobenzylamines (13; R = H or Me) and (14),



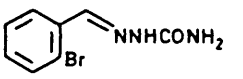
(9)



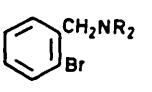
(10)



(11)



(12)



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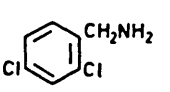
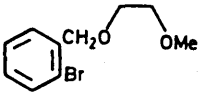


(14)



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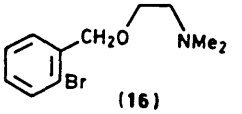
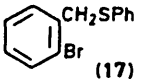
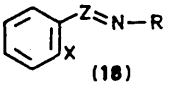


(16)



(17)

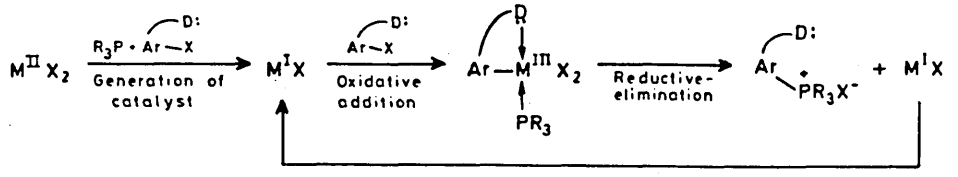


(18)

whilst having a nitrogen atom in the same relative position as in the reactive Schiff's bases, also fail to undergo conversion to the related phosphonium salts. Replacement of nitrogen by *either* oxygen, as in *o*-bromobenzyl alcohol, and the ethers (15) and (16), *or* by sulphur, as in (17), has no effect in promoting the substitution reactions, these compounds being inert on prolonged reflux in ethanol with triphenylphosphine, in the presence of nickel(II) ion.

Thus it would appear that such metal-ion promoted substitution reactions require a very specific template of type (18; Z = CH or N; R = non-sterically crowded alkyl or aryl). It is of interest to note that the reactions of the diarylazo template systems (1)[6] appear to be much less sensitive to the presence of additional donor centres *e.g.* (1; R^2 = NHCOMe) than those of the Schiff's bases, and also that the reactions of the former are catalysed by both copper(II) acetate and nickel(II) bromide, whereas nickel(II) is required specifically for the reactions of the Schiff's bases. Clearly some very subtle co-ordination chemistry is involved in these reactions. It is highly probable that electron-transfer processes[11] are also involved, in which the metal ion is initially reduced to a lower oxidation state, *e.g.* Ni^I (the active catalytic species) which then undergoes a co-ordination template-assisted oxidative insertion into the carbon-halogen bond, followed by formation of the phosphorus–carbon bond in a reductive-elimination of the phosphonium salt, with regeneration of the catalyst, as in the Scheme.

Whereas the reduction of copper(II) to copper(I) by phosphorus(III) compounds is well-known,[12] the related reduction of nickel(II) to nickel(I) in the absence of an additional reducing agent is less well-documented. However, it is known that nickel(I) complexes are formed in the reactions of certain nickel(II) halides with polydentate phosphines,[13,14] and also that the nickel(0) complex $[Ni\{(EtO)_3P\}_4]$ is formed when nickel(II) chloride is heated in triethylphosphite.[15] Oxidative-



Scheme.

addition of aryl halides to nickel(0) and nickel (I) species is now well established,[16–18] as is also the formation of arylphosphonium salts from arylnickel(II) and arylnickel(III) intermediates.[18,19] In the reactions of the above *o*-halogeno Schiff's bases, we have observed that the rate of phosphonium salt formation increases rapidly when the Schiff's base is treated with the nickel(I) complex $[Ni(Ph_3P)_3Br]$, (accessible by reduction of $[Ni(Ph_3P)_2Br_2]$ with sodium borohydride in ethanol).[20] This result lends some support to the above suggestion of an *in-situ* reduction of the metal from the +2 oxidation state, in which intramolecular co-ordination involving the imino nitrogen of the Schiff's base has a key role in stabilising the lower oxidation state and in promoting the subsequent reactions leading to phosphonium salt formation.

Experimental

^{13}C N.m.r. spectra were recorded on JEOL PFT-100 and Bruker AM-250 spectrometers at 25.15 MHz and 62.9 MHz respectively. Chemical shifts are reported on the δ scale with respect to tetramethylsilane (5% w/v) as an internal standard in deuteriochloroform. Coupling constants are reported in Hz and are accurate to ±0.73 Hz. ^{31}P N.m.r. spectra were recorded on a Bruker AM-250 at 101.3 MHz. Chemical shifts are reported with respect to 85% orthophosphoric acid as an external standard; shifts to high frequency are positive in sign. All chemical shifts are accurate to ±0.1 p.p.m. ^1H N.m.r. spectra were recorded on a Bruker WP80 SY spectrometer at 80 MHz. Chemical shifts are reported on the δ scale with respect to tetramethylsilane as an internal standard in deuteriochloroform. High resolution mass spectra were recorded using a Kratos MS80 mass spectrometer coupled to a DS/55 data system, with perfluorokerosene as the reference compound.

Preparation of Potential Templates.—The following compounds were prepared as previously described: 2-Bromobenzyl-*N*,*N*-dimethylamine,[21] 2-bromobenzaldehyde semi-carbazone,[22] 2-bromobenzyl phenylsulphide,[23] (2-fluorobenzylidene)aniline,[24] *N*-(2-chlorobenzylidene)-4-methoxyaniline,[25] *N*-(2-bromobenzylidene)-4-methoxyaniline,[26] *N*-(2-iodobenzylidene)-4-methoxyaniline,[27] *N*-(2,4-dichlorobenzylidene)-4-methoxyaniline,[28] 2-bromobenzaldehyde oxime,[29] 2-(2-bromobenzyloxy)-*N*,*N*-dimethylethylamine.[30] 2-Bromobenzylamine and 2,4-dichlorobenzylamine were obtained commercially. The following compounds appear to be new:

2-(2-*Bromobenzyloxy*)-1-*methoxyethane* (**15**). To a solution of sodium (0.7 g) in 2-methoxyethanol (25 cm^3) was added 2-bromobenzyl bromide (5 g), and the resulting mixture heated under reflux for 2 h. The cooled reaction mixture was then poured into water (100 cm^3) and the product extracted with chloroform (4 × 15 cm^3). Evaporation of the dried chloroform extract gave an oil which was purified by distillation under reduced pressure to give the *bromo ether* (4.16 g, 85%), as a pale yellow liquid, b.p. 98 °C at 0.4 mmHg (Found: C, 48.95; H, 5.45. $C_{10}H_{13}BrO_2$ requires C, 48.95; H, 5.35%); δ_H = 4.2—4.8 (m, 4 × ArH), 6.5 (2 H, s), 7.2 (4 H, br s), and 7.4 (3 H, s).

Schiff's Bases. These were prepared by heating together equimolar quantities of the 2-halogenoaryl carbonyl compound and primary amine in *either* ethanol *or* toluene, in the presence of a trace of toluene-*p*-sulphonic acid as a catalyst, (with removal of liberated water using a Dean-Stark trap). In most cases, the products crystallised on cooling, and were purified by further recrystallisation. In a few cases, the products were oils which could not be purified sufficiently for satisfactory microanalysis and so were characterised by ^1H n.m.r. and high resolution mass spectrometry. The ^1H n.m.r. spectra of all of these compounds exhibited a characteristic signal at $\delta \simeq 8.5$—9.0 due to the azomethine proton.

2,4-*Dibromo*-N-(4-*methoxybenzylidene*)*aniline* (**9**). This had m.p. 87—88 °C (from EtOH) (Found: C, 45.6; H, 2.95; N, 3.7; $C_{14}H_{11}Br_2NO$ requires C, 45.55; H, 3.0; N, 3.8%); δ_H 8.2 (1 H, s), 8.1—6.4 (7 H, m), and 3.85 (3 H, s).

2,4-*Dichloro*-*N*-(4-*methoxybenzylidene*)*benzylamine* (**10**). This had m.p. 41 °C (from EtOH) (Found: C, 61.25; H, 4.45; N, 4.75. $C_{15}H_{13}Cl_2NO$ requires C, 61.2; H, 4.45; N, 4.75%); δ_H 8.3 (1 H, s); 7.9—6.7 (7 H, m), 4.8 (2 H, s), and 3.8 (3 H, s).

N-(2-*Bromobenzylidene*)*benzylamine* (**5**; R = $PhCH_2$), isolated as an oil [Found: $M^+(^{81}Br)$, 275.0148. $C_{14}H_{12}BrN$ requires $M(^{81}Br)$, 275.0134]; δ_H 8.75 (1 H, s), 8.2—7.0 (9 H, m), and 4.8 (2 H, s).

N-(2-*Bromobenzylidene*)-*t*-*butylamine* (**5**; R = Bu^t). This was isolated as an oil [Found: $M^+(^{81}Br)$, 241.0295. $C_{11}H_{14}BrN$ requires $M(^{81}Br)$, 241.0291]; δ_H 8.1 (1 H, s), 8.15—7.10 (4 H, m), and 8.3 (9 H, s).

N-(2-*Bromobenzylidene*)-1-*phenylethylamine* [**5**; R = CH(Me)Ph]. This was isolated on an oil [Found: $M^+(^{81}Br)$, 289.0312. $C_{15}H_{14}BrN$ requires $M(^{81}Br)$, 289.0290]; δ_H 8.75 (1 H, s), 8.25—7.95 (1 H, m), 7.7—6.9 (8 H, m), 4.6 (1 H, q), and 1.6 (6 H, d).

N-(2-*Bromobenzylidene*)-2-*hydroxyethylamine* (**5**; R = CH_2CH_2OH). This was isolated as an oil [Found: $M^+(^{81}Br)$, 228.9926. $C_9H_{10}BrNO$ requires $M(^{81}Br)$ 228.9925]; δ_H 8.6 (1 H, s), 7.95 (1 H, m), 7.6—7.0 (3 H, m), and 4.8 (4 H, m).

N-(2-*Bromobenzylidene*)-2-(2-*pyridyl*)*ethylamine* [**5**; R = $CH_2CH_2(2\text{-}C_5H_4N)$]. This was isolated as an oil [Found: $M^+(^{81}Br)$, 290.0252. $C_{14}H_{13}BrN_2$ requires $M(^{81}Br)$, 290.0243]; δ_H 8.55 (1 H, s), 7.95 (1 H, m), 7.7—6.7 (7 H, m), 4.05 (2 H, t), and 3.2 (2 H, t).

2-*Amino*-N-(2-*bromobenzylidene*)*benzo*[b]*thiazole* (**5**; R = 2-C_7H_4NS). This was obtained as yellow crystals, m.p. 196—197 °C (from toluene) [Found: $M^+(^{81}Br)$, 317.9674. $C_{14}H_9BrN_2S$ requires $M(^{81}Br)$, 317.9651].

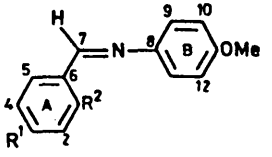
2-*Amino*-N-(2-*bromobenzylidene*)*benzo*[b]*imidazole* (**5**; R = 2-$C_7H_5N_2$). This was obtained as pale yellow crystals, m.p. 208 °C (from EtOH) (Found: C, 56.0; H, 3.35; N, 14.0. $C_{14}H_{10}BrN_3$ requires C, 56.0; H, 3.35; N, 14.0%).

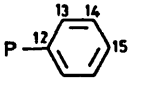
N,N'-*Bis*-(2-*bromobenzylidene*)*ethane*-1,2-*diamine* (**7**). This was obtained as white crystals, m.p. 99 °C (from EtOH) (Found: C, 48.85; H, 3.75. $C_{16}H_{14}Br_2N_2$ requires C, 48.75; H, 3.60%); δ_H 8.65 (2 H, s), 8.0 (2 H, m), 7.7—7.0 (6 H, m), and 4.05 (4 H, s).

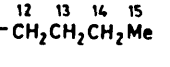
N,N'-*Bis*-(2-*bromobenzylidene*)*biphenyl*-2,2'-*diamine* (**8**). This was obtained as pale yellow crystals, m.p. 108 °C (from EtOH) (Found: C, 60.25; H, 3.45; N, 5.30. $C_{26}H_{18}Br_2N_2$ requires C, 60.25; H, 3.45; N, 5.40%); δ_H 8.5 (2 H, s), and 8.0—6.5 (16 H, m).

N-[1-(2-*Bromophenyl*)*ethylidene*]-4-*methoxyaniline* (**3**; R^1 = Me, X = Br, Y = H). This was isolated as an oil, *m/z* 305

Table. ^{13}C N.m.r. spectroscopic data for Schiff's bases and related phosphonium salts.







Compd.	R^1	R^2	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	OMe	C-12	C-13	C-14	C-15	δ_P	Other carbons
A	H	H	128.6[a]	128.5[a]	130.9	128.5[a]	128.6[a]	136.3	158.2	144.8	122.1	114.3	158.2	55.4						
B		Cl	133.6[a]	131.7[b]	129.8[b]	128.4[b]	127.0[b]	135.8[a]	154.5	144.7	122.4	114.4	158.6	55.4						
C		Br	125.8	133.1[a]	131.9[a]	128.7[a]	127.6[a]	134.7	156.9	144.4	122.5	114.4	158.6	55.4						
D		PPh_3	114.0	138.9[a]	132.1	136.4	136.1[a]	140.4	153.0	139.4	121.6	114.2	159.3	55.4	122.5	133.0	129.9	134.0	25.9	
			(93)	(12)	(14)	(3)	(9)	(4)							(95)	(10)	(13)	(3)		
E		PBu_3	113.8	135.7[a]	131.5	134.3	135.4[a]	149.6	156.0	140.9	122.0	114.6	159.3	55.2	22.0	24.2	23.3	13.0	33.7	
			(76)	(9)	(12)	(3)	(8)	(5)							(52)	(5)	(17)			
F	Cl	H	129.6[a]	128.9[a]	135.0[b]	128.9[a]	129.6[a]	136.9[b]	156.4	114.5	122.2	144.4	158.5	55.4						
G		Cl	137.0[a]	127.5	136.1[a]	129.2[b]	129.7[b]	132.0[a]	153.0	114.1	122.4	144.4	158.7	55.4						
H		PPh_3	116.2	138.0[a]	137.9	136.1	137.6[a]	138.9	152.1	138.4	121.8	114.2	159.3	55.3	121.9	132.9	130.0	134.3	25.5	
			(92)	(13)	(18)	(2)	(10)	(3)							(96)	(9)	(13)	(3)		
I		PBu_3	116.8	137.6[a]	137.7	134.8	134.9[a]	138.8	155.3	141.0	122.7	115.1	160.0	55.6	22.6	24.8	23.7	13.5	34.5	
			(73)	(9)	(14)	(0)	(14)	(4)							(50)	(4)	(17)			
J	Br	H	125.3	131.9[a]	129.8[a]	131.9[a]	129.8[a]	135.4	156.3	144.5	122.2	114.4	158.5	55.4						
K	H	PPh_3	113.8	138.4[a]	132.1	136.0	136.1[a]	139.3	154.9	145.9	119.3	128.4	126.8	*	121.6	132.2	129.4	133.6	26.6	
			(92)	(12)	(14)	(0)	(14)	(4)							(96)	(9)	(13)	(3)		
L	H	PPh_3	124.3†	139.3[a]	132.3	136.7	*a*	141.3	157.2‡	137.0	120.2	113.6	161.9	55.2					21.7	17.0 (Me)
			(98)	(14)	(15)	(3)		(3)												
M	H§	PPh_3	113.9	138.5	131.9	136.1	135.3	139.6	157.6	135.4	128.1[a]	128.2[a]	126.9		122.1	132.3	129.6	133.7	25.5	61.4 (CH_2)
			(93)	(12)	(14)	(3)	(12)	(4)												

Superscript letters: assignment interchangeable. * No OMe substituent on ring, (ref. 33). † Signal broad at ambient. ‡ Schiff's base carbon also has a methyl substituent. § Benzyl substituent at Schiff base nitrogen. ^{31}P–^{13}C coupling constants in parentheses.

[M^+(^{81}Br)]. Due to coincidence of reference signals, it was not possible to record an accurate mass for the molecular ion. The ^{1}H n.m.r. spectrum indicated that a mixture of isomers was present: δ_H 7.8—6.4 (8 H, m), 3.8 and 3.7 (both s, MeO), and 2.6 and 2.45 (both s, Me). This substrate was characterised by its subsequent conversion to the related phosphonium salt (see below).

Reactions of Schiff's Bases with Phosphines: General Procedure.—The Schiff's base (1 mmol), tertiary phosphine (2 mmol) and anhydrous nickel(II) bromide (0.1 mol. equiv.) were heated together under reflux in ethanol (10 cm^3) in a nitrogen atmosphere for 5—8 h, and the progress of the reaction was monitored by t.l.c. [Kieselgel; $CHCl_3$–EtOH (80:20) as the eluant]. The reaction mixture was then poured into water (50 cm^3) containing KBr (0.5 g), and extracted with ether (2 × 20 cm^3) in order to remove non-ionic impurities. The aqueous layer was then extracted with chloroform (3 × 10 cm^3). The chloroform layer was dried ($MgSO_4$) and evaporated. The oily residue was then triturated several times with dry ether until it solidified. The phosphonium salt was then recrystallised from chloroform–ethyl acetate (except as stated otherwise). The following salts were characterised (^{31}P and ^{13}C data are presented in the Table).

N-(4-*Chloro*-2-*triphenylphosphoniobenzylidene*)-4-*methoxyaniline bromide* (**4**; R^1 = H, R^2 = Ph; Y = Cl, X = Br). M.p. >267 °C (decomp.) (Found: C, 65.6; H, 4.3; N, 2.55. $C_{32}H_{26}BrClNOP$ requires C, 65.45; H, 4.45; N, 2.4%); $\delta_H(CDCl_3)$ 8.9 (1 H, s), 8.85—6.8 (18 H, m), 6.7—6.0 (4 H, deceptively simple $[AX]_2$ system), and 3.70 (3 H, s).

N-(2-*Triphenylphosphoniobenzylidene*)*benzylamine bromide* (**6**). This was characterised as the *tribromomercurate*(II) salt, m.p. 205—207 °C (from $CHCl_3$) (Found: C, 42.3; H, 2.85; N, 1.4. $C_{32}H_{27}Br_3HgNP$ requires C, 42.85; H, 3.05; N, 1.55%); $\delta_H(CDCl_3)$ 8.55 (1 H, s), 8.5—6.4 (24 H, m), and 3.9 (2 H, s).

4-*Methoxy*-N-(α-*methyl*-2-*triphenylphosphoniobenzylidene*)-*aniline bromide* (**4**; R^1 = Me, R^2 = Ph; Y = H, X = Br). M.p. >265 °C (decomp.) (Found: C, 69.5; H, 5.15; N, 2.45. $C_{33}H_{29}BrNOP$ requires C, 69.95; H, 5.15; N, 2.45%); $\delta_H(CDCl_3)$ 8.60—8.52 (1 H, m), 8.27—8.18 (1 H, m), 7.84—7.12 (15 H, m), 6.5—5.1 (4 H, deceptively simple $[AX]_2$ system), 3.69 (3 H, s), and 2.34 (3 H, s).

4-*Methoxy*-N-(2-*triphenylphosphoniobenzylidene*)*aniline bromide* (**4**; R^1 = H, R^2 = Ph; Y = H; X = Br). M.p. 249 °C (Found: C, 67.45; H, 5.1; $C_{32}H_{27}BrNOP{\cdot}H_2O$ requires C, 67.35; H, 5.1%); $\delta_H(CDCl_3)$ 8.6 (1 H, s), 8.5—7.0 (19 H, m), 6.7—5.9 (4 H, deceptively simple $[AX]_2$ system), and 3.7 (3 H, s).

4-*Methoxy*-N-(2-*tributylphosphoniobenzylidene*)*aniline bromide* (**4**; R^1 = H, R^2 = Bu; Y = H; X = Br). M.p. 103—105 °C (Found: C, 63.5; H, 8.05; N, 2.8. $C_{26}H_{39}BrNOP$ requires C, 63.40; H, 8.0; N, 2.85%); $\delta_H(CDCl_3)$ 8.9 (1 H, s), 8.25—7.82 (4 H, m), 7.45—6.97 (4 H, deceptively simple $[AX]_2$ system), 3.87 (3 H, s), 3.02—2.80 (6 H, m), 1.60—1.40 (12 H, m), and 0.95—0.84 (9 H, m).

N-(4-*Chloro*-2-*tributylphosphoniobenzylidene*)-4-*methoxyaniline bromide* (**4**; R^1 = H; R^2 = Bu; Y = Cl; X = Br). M.p. 198—199 °C (Found: C, 58.95; H, 7.20; N, 2.57. $C_{26}H_{38}BrClNOP$ requires C, 59.24; H, 7.25; N, 2.65%); $\delta_H(CDCl_3)$ 8.9 (1 H, s), 8.4—7.55 (3 H, m), 7.5—6.8 (4 H, deceptively simple $[AX]_2$ system), 3.85 (3 H, s), 3.3—2.7 (6 H, m), 1.8—1.2 (12 H, m), and 1.1—0.7 (9 H, m). The salt (200 mg) was dissolved in ethanol (3 cm^3) and treated with aqueous sodium hydroxide (30% w/v; 2 cm^3), and the resulting mixture allowed to stand at room temperature for 7 days. It was then poured into water (15 cm^3) and the mixture extracted with ether (2 × 10 cm^3). The dried ether extract was evaporated and the residue recrystallised from ethanol to give *N*-(4-chlorobenzylidene)-4-methoxyaniline, m.p. 123 °C, identical with an authentic sample.

^{13}C *N.m.r. Spectroscopic Data.*—The ^{13}C n.m.r. chemical shifts of the parent Schiff's bases and related phosphonium salts are reported in the Table. Signals were assigned using the standard techniques of Spin Echo Fourier Transform (S.E.F.T.), (with a delay time of $1/J$).[31,32]

Ring A. With one exception (compound L), all the signals are sharp, and, in the case of the phosphonium salts, exhibited coupling to phosphorus. As noted previously in related *o*-phosphoniodiarylazo derivatives (**2**),[6] the substituent *ortho* to phosphorus in the phosphonium salts has a marked effect on the value of $^2J_{PC}$.

Compound L, in which the Schiff base carbon bears a methyl substituent, shows a marked chemical shift change of *ca.* 8 p.p.m. for C-1 with respect to the other triphenylphosphonium salts. Furthermore, this signal is broader and there is a signal missing for one of the aryl ring-carbons. It is probable that the methyl substitution causes some form of restricted ring rotation and this would account for the broadening of the C-1 signal; also as seems likely, the missing signal corresponds to C-5 which should also be broadened and would account for its loss.

For compounds H and I, it is possible that the phosphonium salt could be formed either *ortho*- or *para*- to the Schiff's base substituent on the aryl ring. Substitution parameters for $\overset{+}{P}Ph_3$ and $\overset{+}{P}Bu_3$ on compound B show that a *para*- phosphonium salt should give a chemical shift for C-5 of 129 p.p.m. whilst an *ortho*-phosphonium salt of compound F gives a chemical shift of 113 p.p.m. Whilst multiple substitution in rings can give rise to large errors when using substitution parameters, the lack of any CH resonance in compounds H and I below 134 p.p.m. and the fact that C-6 always exhibited a coupling constant $^2J_{PH}$ of 4—5 Hz would strongly indicate that the phosphonium salt has been formed *ortho*- to the Schiff's base substituent.

Ring B. Unlike the *ortho*- phosphoniodiarylazo derivatives (**2**), no broadening of the aryl carbon signals is observed in any of the compounds studied. Changes in chemical shift of C-9, C-10, and C-11 are very small. Variations in C-8 are more marked and probably reflect changes in the relative orientation of the rings due to variation in the bulk of the *ortho*-substituent on Ring A.

Schiff's Base Carbon. Variations in the chemical shift of C-7 are not large with the exception of the triphenylphosphonium salts, again reflecting a steric bulk interaction.

Other Carbon Signals. The signals for the other carbons in the molecule—methoxy, phenyl, and butyl side chains, show no abnormal chemical shift behaviour and correspond closely to values found for the *ortho*- phosphoniodiarylazo derivatives.[6]

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A Kinetic Template Effect in the Nickel-catalysed Reactions of a 2-(2-Bromophenyl)benzimidazole with Tertiary Phosphines. *X*-Ray Crystal Structure of Triphenyl-{2-[1-(2-bromobenzyl)benzimidazol-2-yl]phenyl}phosphonium Bromide Di(chloroform) Solvate

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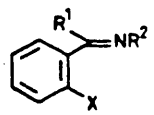
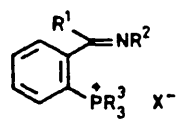
We report that the reactions of 1-(2-bromobenzyl)-2-(2-bromophenyl)benzimidazole (**8**) in refluxing ethanol with triphenyl- and tributyl-phosphine in the presence of nickel(II) bromide proceed with regiospecific replacement of the bromide atom of the 2-bromophenyl substituent to form the respective arylphosphonium salts (**9**; R = Ph or Bu), the 2-(2-bromophenyl)benzimidazole moiety acting as a 'kinetic co-ordination template' which directs the course of substitution. An *X*-ray diffraction study of the salt (**9**; R = Ph) is also reported.

The reactions of aryl halides with tertiary phosphines to form arylphosphonium salts usually only proceed at high temperatures (150–200°C) and in the presence of a transition metal halide, *e.g.* $Ni^{II}Br_2$, as catalyst.[1-4] In recent work,[5] we have shown that when the *ortho*-halogenoimines (**1**; R^1 = H or Me; R^2 = aryl or benzyl; X = Cl, Br, or I) are heated *in ethanol* with a tertiary phosphine in the presence of a nickel(II) halide catalyst, the *ortho*-halogen is replaced to form the related arylphosphonium salts (**2**; R^1 = H or Me; R^2 = aryl or benzyl; R^3 = Rh or Bu; X = Cl, Br or I). If the halogen is present in the position *meta* or *para* to the azomethine group, the reaction does not take place.



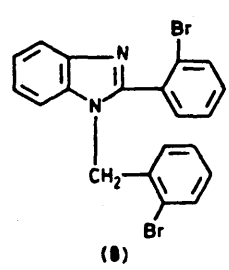
(**1**)



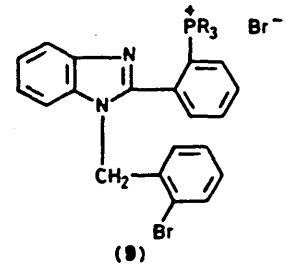
(**2**)

We have suggested that these reactions involve the operation of a kinetic template effect in which metal-ion promoted replacement of the halogen *ortho* to the amino group is assisted by co-ordination of the metal to the imino nitrogen atom. We have also shown that introduction of a second donor atom or group into the substituent R^2 present at the imino nitrogen of related Schiff's bases inhibits these reactions, presumably owing to the diversion of the metal ion in other modes of co-ordination.

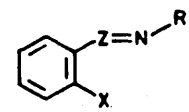
During the course of the above study, the benzimidazole (**8**) was isolated, unexpectedly, from the reaction of *o*-bromobenzaldehyde (2 mol) and *o*-phenylenediamine (1 mol) in ethanol. In the light of our earlier work on metal ion-catalysed reactions of potential template aryl halides with tertiary phosphines, it was therefore of considerable interest to investigate the related reactions of the benzimidazole (**8**) in which the imine-like nitrogen of the ring system is in the same relative position to the halogen as that in the *o*-halogenobenzaldimines (**1**). On heating under reflux in ethanol with triphenylphosphine or tributylphosphine, in the presence of nickel(II) bromide, the benzimidazole (**8**) was coverted into the related phosphonium salts (**9**; R = Ph or Bu).



(**8**)



(**9**)



(**10**)

As in the case of the related reactions of the *o*-halogenobenzaldimines (**1**), the above reactions are only catalysed by the presence of nickel(II) halides. The substitution reactions do not proceed in the presence of copper(II) acetate, which has been shown to be an effective catalyst in the related reactions of *o*-bromodiarylazo dyestuffs with tertiary phosphines[6] and also with triethyl phosphite.[9,10]

The regiospecificity of the halogen-replacement reaction in the benzimidazole (**8**) supports our earlier suggestion[5] that active template substrates should be of the general type (**10**; Z = CR or N) in which the halogen, sp^2-hybridised nitrogen, and metal ion may be involved in an initial six-membered cyclic association. Clearly, the *o*-bromobenzyl substituent present at the pyrrole-like nitrogen in (**8**) is far removed from the active site, and is not involved in the substitution reaction.

X-Ray Structural Study of Triphenyl-{2-[1-(2-bromobenzyl)benzimidazol-2-yl]phenyl}phosphonium Bromide (**9**; R = Ph) *[as a Di(chloroform) Solvate]*. – *Crystal data*. $C_{40}H_{31}Br_2Cl_6N_2P$; M_r = 942.9. Triclinic, space group $P\bar{1}$, a = 11.125(6), b = 13.282(8), c = 13.947(4) Å, α = 96.78(4), β = 85.24(5), γ = 75.96(1)°, U = 1972.2 Å^3, Mo-K_α radiation (λ = 0.71069 Å), D_m = 1.49, C_c = 1.58 g cm^{-3}, Z = 2, μ(Mo-K_α) 24.43 cm^{-1}, F(000) = 944. R = 0.078 (R' = 0.082) for 3137 observed diffractometer data. The structure was solved by the heavy-atom method. The geometry around the phosphorus atom (Figure) is approximately tetrahedral with bond angles in the range 107–114°. There does not appear to be any significant interaction between the bromide ion and the cation, the closest P$^+$···Br$^-$ distance being 4.5 Å. Omitted from the crystal structure for clarity are two chloroform molecules. It is thought that the hydrogen atoms from these two molecules are hydrogen bonded to the bromide anion [bond distances are Br(2)-H(9) 2.50 and Br(2)-H(10) 2.55 Å respectively] and that these molecules in turn form discrete channels running through the crystal lattice.

Techniques used: ^{1}H and ^{31}P n.m.r, mass spectrometry, *X*-ray diffraction

* To receive any correspondence.

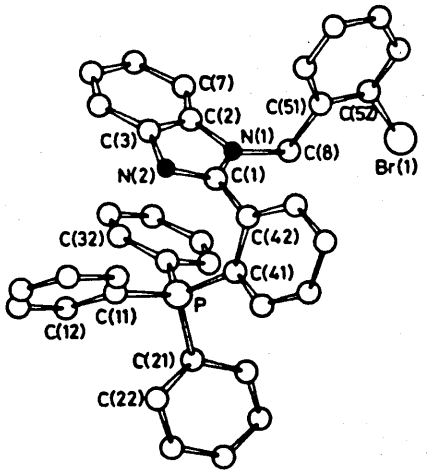


Figure Structure of the triphenyl-[2-[1-(2-bromobenzyl)-benzimidazol-2-yl]phenyl]phosphonium cation

Table 1: Final fractional co-ordinates with estimated standard deviations

Table 2: Selected bond distances for compound (**9**; R = Ph)

Table 3: Selected bond angles for compound (**9**; R = Ph)

Appendix: Thermal parameters for compound (**9**; R = Ph)

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